GENERAL LIBRARY
MAY 11 1912
UNIV. OF MICH.

BULLETIN

OF

THE JOHNS HOPKINS HOSPITAL

Entered as Second-Class Matter at the Baltimore, Maryland, Postoffice.

Vol. XXIII.—No. 255.] BALTIMORE, MAY, 1912. [Price, 25 Cents

CONTENTS.

	PAGE
The Effect of Extensive Resections of the Small Intestine. (Illustrated.) By Joseph Marshall Flint, M. D.	127
The Behavior of the Blood Platelets in Toxemias and Hæmorrhagic Disease: A Preliminary Report. By W. W. Duke, M. D.	144
An Alveolar Tumor of the Carotid Gland with Sarcomatous Transformation. (Illustrated.) By Paul G. Woolley, M. D., and Frank Fee, M. D.	146
Notes on New Books	151
Books Received.	157

THE EFFECT OF EXTENSIVE RESECTIONS OF THE SMALL INTESTINE.

By Joseph Marshall Flint, M. D.,
Professor of Surgery, Yale University.

(From the Surgical Laboratory of Yale University, and the Continuous Surgical Service of the New Haven Hospital.)

Since the appearance of a preliminary communication[1] on this subject, the completion of more experimental work and the appearance of several important papers in the current literature have made it seem desirable to republish it with the inclusion of several new cases, tending to modify, to a certain extent, the conclusions that had been drawn concerning them.

In these days of aggressive surgery, it is important to know the limits of resection of various organs and tissues and, particularly, to be familiar with the response which the organism makes to the loss of large portions of them by reason of either surgical interference or disease. Response to injury or destruction of organs or tissues, either in whole or in part, may be met by several compensatory processes, of which the regeneration of the lost or injured portion represents the most perfect type of compensatory action. In other instances, a hypertrophic process may result either in the remaining portion of the organ or tissues, or sometimes in its mate in case the structure is bilateral.

In general, we now distinguish two kinds of hypertrophy: functional, when a part becomes enlarged through use; and compensatory, when an organ or a part of it is removed and the remainder, or its mate, hypertrophies in consequence. Naturally, the compensatory hypertrophies may also be viewed as the result of extra work caused by the removal of the organs, or a part of them. Although superficial, this distinction between the two processes is not unhelpful, as, in the compensatory hypertrophy, we are usually dealing with an adaptation to neutralize a pathological condition or to offset the effect of an injury. A further useful morphological differentiation of the hypertrophic process was introduced by Virchow, who speaks of hypertrophy in the sense of an enlargement of the cells, and of hyperplasia as indicating an increase of the number of cells of which the tissue or organ is composed.

Still another type of compensation, which seems to be vicarious in nature, is where one organ may show compensatory action on behalf of another from which it may be, so far as we know, physiologically different. Of this type of compensation we know least, although it will form one of the most interesting chapters in the future development of experimental medicine.

To determine which of these compensatory processes was involved, some eleven years ago, at the suggestion of Dr. F. P. Mall, Dr. R. F. Rand and myself began to study the effects of removing large portions of the small intestine. Our period of collaboration, unfortunately, ended with the completion of the operations, and since that time I have only had sporadic opportunities to finish the study of the preparations which we obtained, and to perform such new experiments as the progress of the work demanded.

[1] Flint. Trans. Conn. State Med. Soc. 1910, 283.

Methods and Materials.

Dogs were selected for experiments, partly because of their well-known resistance to operative procedures, but largely because the finer anatomy of the intestine in the dog has been exhaustively studied by numerous investigators. The dogs were prepared for operation with scrupulous care, and all of the usual aseptic precautions were taken. After a thorough disinfection of the skin, the abdominal cavity was opened. The whole movable portion of the small intestine, that is to say, the combined jejunum and ileum, was then delivered into the wound. In this way, the duodenum and a part of the jejunum was excluded from the operation, owing to their fixation and the anatomical relations, which made it impossible either to resect or to measure them for the purpose of control in determining whether there had been a regeneration in the portion of the intestine left in the body. Accordingly, it was our custom, during the first operations, to mark the upper end of the jejunum by a black stitch and, from this point, the measurements of the intestines were taken. These stitches proved, however, entirely too uncertain and, finally, we had recourse to a subserous injection of lampblack, sterilized in salt solution, which gave an indelible tatoo, forming a permanent and terminal landmark from which the combined jejunum and ileum could be measured. As a preliminary stage of the operation, it was our custom to measure the whole of the small intestine from the tatoo mark on the jejunum to the cæcum. Owing to the great elasticity of the gut, this measurement could not be made absolute; so one of us, the writer, always measured the intestine by applying as nearly as possible the same tension upon the gut, while protecting it from the longitudinal shrinking that follows its exposure to the air, by means of gauze pads soaked in warm salt solution. Although there is always a slight error in the measurements, the method, nevertheless, is relatively accurate, as the determinations were always duplicated and the mean used as the determined length. In two such measurements of the intestine, there was rarely a discrepancy of more than 30 cm., which would place the average error in determining the length of the whole portion of the gut with a free mesentery, at about 15 cm. As the measurements were taken, marks and measurements were made to determine the position of the upper and lower points of the portion to be resected, which gave us an additional landmark in the suture to determine whether there was a lengthening of the segment of the intestine left at operation. The mesenteric vessels were then tied, and a fan-shaped piece of mesentery cut leading to the points of section. After resection of a segment, the continuity of the intestine was re-established by an end-to-end anastomosis. For purposes of control and comparison, the resected portion of the intestine, after the completion of the operation, was stretched to its measured length in the body, opened, washed, and rolled around a glass cylinder in such a way as to keep the mucosa from being injured while the specimen was being fixed and hardened in formalin.

In a later series of experiments, a functional resection of the intestine was accomplished by means of a short-circuiting lateral anastomosis with the invagination of the upper end of the lower segment of the gut. To prevent intussusception, this end was stitched to the abdominal wall. Thus the functionless portion remained in the abdominal cavity, to be compared at autopsy with the measurements taken at operation. Furthermore, an absolute comparison of the short-circuited segment with that retaining its functional activity is possible by means of the distension of both segments simultaneously with an equivalent hydraulic pressure. Dogs Nos. 12, 13 and 14 are examples of this series.

The metabolic disturbances following the resection of the intestine were studied by Drs. Erlanger and Hewlett, to whom were loaned Dogs Nos. 2, 9 and 10, and whose results will be considered in detail later. My colleague, Professor Underhill, determined the metabolic changes in Dogs Nos. 12, 13 and 14, upon which a short-circuiting operation was done. For the morphological changes, I have used all of the microscopic methods which might throw any light upon the changed structure of the intestine. In order to have an absolute method of comparison in studying any modifications that might occur in the mucosa, the Born wax plate reconstruction method was employed. Further details concerning the technique will be given, as they may have a bearing on the interpretation of the results.

Experiments.

The general results of the operations for the purpose of our study may be collected in the following table:

TABLE

Dog No.	Sex	Weight, pounds	Length of ileum and jejunum	Resected	% Removed	Table: Whole length small intestine	Table: % Removed.	Table: Days lived	Result	Remarks—Cause of death
1	F	25	287	55	19					
1*	F	29	332	176	61	348	66	110	Recovery	Killed for observation.
2	M	33	332	80	34					
2*	M	33	175	84	36	301	54	451	Recovery	Killed for observation.
3	F	27	316	132	43	...	..	23	Died	Pneumonia.
4	M	38	291	209	72	...	..	32+	Recovery	Escaped from dog house in good condition.
5	M	14	227	183	80	252	70	9	Died	Ileus from adhesions.
6	F	29	323	295	91	...	..	10	Died	Omental hernia, peritonitis. Infection of abdominal wound.
7	M	20	198	174	87	219	79	9	Died	[redacted]al hernia, peritonitis. Infection of abdominal wound.
8	F	22	339	288	85	...	..	6	Died	Omental hernia, peritonitis. Infection of abdominal wound.
9	F	29	357	298	83	458	65	220	Recovery	Died during metabolism experiments.
10	F	23	289	238	81	334	70	322	Recovery	Killed for observation.
11	M	31	425	364	85	...	..	17	Died	Abscess about suture.
12†	F	..	...	237	..	323	73	213	Recovery	Killed for observation.
13†	F	..	525	350	66	...	..	...	Recovery	Killed for observation.
14†	F	..	412	162	39	...	..	...	Recovery	Killed for observation.

* Second operation.
† Intestine not resected. Segment short-circuited by enteroenterostomy.

It may be well to recall, however, that the measurements are only approximate, as it is impossible to determine absolutely the length of an elastic organ in the body of a living animal. Furthermore, the recorded length is perhaps consid-

erably greater than normal, as the intestine, during the measurement, was put under slight tension to counteract the effect of the action of the longitudinal layer of the *tunica muscularis*.

In all, sixteen operations are recorded, two of them being upon dogs from which a portion of the gut had already been removed. Of the sixteen operations on fourteen dogs, six died from all causes, making a total mortality of 37 per cent. In no case, however, could the reaction of the intestine *per se* be looked upon as the direct or primary cause of death, although it might naturally be considered a contributory factor in reducing the resistance by causing profound metabolic disturbances, as was evidenced by the extreme diarrhœa and loss of weight. From the table and protocols given above, it will be seen that three died from infection resulting from a breaking down of the abdominal wound; one died from ileus in consequence of adhesions about the intestinal suture; one died from pneumonia, and the last from inanition, induced by the metabolism experiments, after living 213 days.

From the general clinical observations[2] on the operated animals, we found that relatively large portions of the small intestine in dogs may be removed without danger to the life of the animal. The maximum is difficult to determine, as the immediate effect of the operation would, no doubt, depend to a great extent on the general condition of the dog at the time the resection was made. But this much can be said: dogs from which about 80 per cent of the combined ileum and jejunum have been removed, or short-circuited (Dogs Nos. 1, 9, 10 and 12) may live indefinitely after the operation. The first effects of the operation give a profuse diarrhœa and loss of weight, from both of which the animal slowly recovers. At the same time, the resection of a smaller amount, *i. e.*, 65 per cent of the entire intestine (Dogs Nos. 9, 12 and 13), may lead, notwithstanding a ravenous appetite and an unlimited diet, to changes which prevent the dog from regaining its former well-nourished condition. In these animals the nutrition may be apparently normal, but they are, nevertheless, so sensitive to diatetic disturbances that a diet or conditions of any severity may introduce a fatal marasmus or enteritis (Dogs Nos. 9, 12 and 13). Young growing animals (Dogs Nos. 3, 8 and 11) apparently do not stand the operation of the removal of large amounts of the intestine as well as older dogs, and those cases (Dogs Nos. 1 and 2) where two operations were performed, that is to say, where the resection was fractional, recovered sooner and with greater ease than where the entire resection was made at one sitting.

METABOLIC EXPERIMENTS.

A number of months after the operations, three dogs, Nos. 2, 9 and 10, were loaned to Drs. Erlanger and Hewlett, who wished to study the effects of shortened intestines upon metabolism. Their results have already appeared in another place, and, from this paper, the following brief summary of their conclusions may be given. In their series, No. 1 corresponds to our No. 2, No. 2 to our No. 10, and No. 3 to our No. 9. Owing to a misunderstanding of our methods of numbering both dogs and operations separately, the corresponding figures are incorrectly given in their paper. When an easily absorbable diet is given, dogs with shortened intestines behave like normal dogs. The fat and nitrogenous content of the fæces may not exceed the normal. Upon increasing the fat in the diet, however, the abbreviation of the intestine shows its influence on the power of absorption. Under these conditions, the percentage of both fat and nitrogenous material in the fæces may reach a fourth of that which is ingested in the diet. Notwithstanding this fact, the animals increased in weight, as relatively a large amount of fat is absorbed. The diminished absorption is simply an index of the effect of resecting large portions of the intestine upon the power of absorption, which may also become evident when the ordinary diet contains many indigestible substances.

Neither in quantity, specific gravity, or nitrogenous content, did the urine of dogs with shortened intestines show any differences from that of normal animals. There was, however, an absolute increase in the quantity of the conjugated sulphates, and a relative increase in the alkaline sulphates, indicating an excess of intestinal putrefaction. In Dog No. 2, from which 54 per cent of the entire small intestine had been removed, there was no marked increase in the quantity of fæces. In Dog No. 10, however, from which 70 per cent had been resected, there was an increase in the amount. In both dogs, the percentage of water in the fæces was equal to or only slightly in excess of that in normal dogs, which is in contrast to the increased percentage in dogs deprived of the large intestine (Harley). The shortening of the intestine has no effect on the absorption of fat when the animal is on a diet poor in fat. As this element of the diet is increased, the fat in the fæces may increase to 25 per cent in a normal dog. This increase, in normal animals, does not markedly accentuate the elimination of nitrogenous material in the fæces. With a shortened intestine there is an increase which may equal an amount double that eliminated by a normal dog, although on a diet poor in fat, there appears to be no great difference between the two.

De Filippi studied the metabolic changes in a dog from which Monari had removed seven-eighths of the small intestine, and in which only one-eighth of the combined ileum and jejunum remained. In this instance, he found that the carbohydrates were completely utilized, that the nitrogen loss was not much greater than in normal dogs, while the continued diminished fat absorption (19 per cent of the total amount ingested recovered in the fæces) made a richer diet for the animal necessary.

Of special importance in connection with the investigations of De Filippi, and of Erlanger and Hewlett are the observations and ileum from two dogs. In one instance he removed the jejunal half, while in the other the lower half was resected. Unlike the other investigators, Diliberti-Herbin was able to conduct experiments on his animals from the time of the

[2] Detailed descriptions of the operations and the post-operative behavior of the animals are included in the preliminary report.

operation and found that the nitrogen and fat excretion varied from 33 per cent to 66 per cent, and remained high for a long period. Ultimately, however, the conditions became more normal.

The results of the metabolism experiments on dogs may be tabulated as follows:

Investigators	Animals	Resection	Percentage of diet nitrogen in fæces	Percentage diet fat in fæces	Perc. diet carbohydrate in fæces
De Filippi	Monari's dog.	190 cm.	Slightly increased	19%	None.
Erlanger and Hewlett	Dogs Nos. 2, 9, 10	51%, 65%, 70%	Normal to 25%	Normal to 25%	No obs.
Diliberti-Herbin	His own.....	50%	33% to 66%	33% to 66%	No obs.
Underhill.....	Dog No. 12...	73%	25.9%	27.7%	None.
Underhill.....	Dog No. 13...	66%	13-19 %	9-34%	None.
Underhill.....	Dog No. 14...	39%	13-16 %	10-14%	None.

From these observations, a number of interesting facts may be found which explain the clinical observations made upon our dogs. The resection of large amounts of the intestine, by diminishing the absorbing surface of the gut, disturbs the balance in the nitrogen and fat absorptions, and leads to an excessive excretion of these elements in the fæces, an increase which may reach two-thirds of the quantity ingested. This accounts for the profuse diarrhœa invariably observed after the operation. Owing to the limited surface of absorption of nutritive substances, the animals are, for a time, forced to consume the nitrogen and fats of their own tissues. Gradually, however, a balance is restored and the excessive excretion of these elements diminishes, until, as Erlanger and Hewlett have shown, the animals, with the exception of an increased intestinal putrefaction, may return to practically normal nutritive conditions. That this restoration of the power of absorption is not complete, however, may be shown by the susceptibility of the dogs to either diets containing indigestible substances, or to diets rich in fats, which lead to diarrhœa, and an excessive excretion of both nitrogenous and fatty elements of the foods. Thus the compensatory mechanism is apparently effectual under favorable conditions of diet and life, but the result is by no means as efficient as the power of absorption of a normal intestine.

In contradistinction to the fat and nitrogen metabolism, however, the carbohydrates in the diet appear to be completely utilized after the compensation has been established (De Filippi, Underhill). It would appear that we have in carbohydrates a more easily assimilated food which can be utilized by animals with shortened intestines, even when fats and nitrogen are excreted in a percentage above normal. In his experiments, Underhill quadrupled the amount of an ordinary carbohydrate diet for a dog of this weight, and still obtained no test. During the metabolism experiments the dog had soft stools, and Underhill observed the water content of the fæces varied between 80 and 84 per cent, which is about 5 to 10 per cent above normal. In a second series of observations carried out upon Dogs Nos. 13 and 14, two weeks after the short-circuiting operation, Underhill obtained no test for carbohydrates in the fæces, indicating an ability on the part of the animals to utilize these easily assimilated foods even during the period when the excretion of the fatty and nitrogenous elements of the diet was at its maximum. The practical significance of these observations should not be overlooked, and will be commented upon later.

The increased putrefaction is undoubtedly due, as Erlanger and Hewlett point out, to the fact that the food remains for a longer period, under the altered circumstances, in the large intestine, exposed to the action of the bacteria, for these dogs, after the compensation is established, have only the normal number of stools per day, and may even be constipated (Dog No. 9).

Besides the experiments on the metabolism of dogs with shortened intestines, there have been several cases reported where observations were made upon the modification of the nutritive processes after extensive resections of the human ileum. An account of these cases is of particular interest, not only for the confirmation which they bring to the observations made upon animals, but because they make it probable that the results obtained from animals may be also applied to man.

Sagini carried on metabolic experiments upon a patient of Ruggi's, a boy of eight years, from whom the latter had removed 330 cm. of small intestine in three sittings. His observations extended over two three-day periods. The first series gave a nitrogen excretion of 5.9 per cent, and a fat excretion of 12.1 per cent, results which were practically normal according to this investigator. The second series yielded a nitrogen excretion of 13.2 per cent and a fat excretion of 15.3 per cent. The averages of these two series of estimations were 9.5 per cent for the nitrogen elimination, and 13.7 per cent for the fat excretion. About the same time, Riva-Rocci studied the metabolism of Fantino's patient, who was sixty years of age, and from whom 310 cm. of the combined ileum and jejunum had been removed. The experiments began eighteen days after the operation, and lasted two weeks. The nitrogen loss varied between 24 and 40 per cent, with an average of 29 per cent, while the fat excretion varied between 17.2 and 34.3 per cent, with an average of 23 per cent. These amounts are somewhat in excess of Riva-Rocci's normal, but, notwithstanding, the patient continued to gain in weight and make an uninterrupted recovery. Riva-Rocci, therefore, concludes that the removal of 300 cm. of the small intestine may effect the metabolism, but not to a sufficient extent to complicate recovery or affect materially the health of the patient. Schlatter removed 192 cm. of gangrenous intestine from an Italian who was suffering from a stab wound of the abdomen. In the metabolism experiments, which Platt carried out in this case, the nitrogen excretion was 10.47 per cent, and the fat excretion 13.93 per cent. The patient recovered and gained in weight. His digestion was considerably impaired, however, and special, easily assimilated food was demanded. Moreover, the patient tired easily, and never succeeded in establishing a true metabolic compensation for the lost intestine. Schlatter concludes, therefore, that the digestive processes may be seriously disturbed by the resection of

more than 200 cm. of small intestine in young persons, unless a rich diet can be provided. Later, Schlatter communicated by letter to Albu the fact that his patient had been, after some two years, so improved that he could live in health upon the ordinary frugal diet of his people (Italians). The improvement had been slow, similar to the gradual recovery of the power of absorption by dogs with shortened intestines.

The case of Lexer, from which 200 cm. of small intestine had been resected, was observed by Albu, who studied the metabolism changes following the operation. The diet which he gave his patient contained 17 grams N., 88 grams fat, 328 grams carbohydrates. Of this amount, the patient lost 10.12 per cent of the diet nitrogen, and 10.1 per cent of the fat in the fæces. The indican was normal in the urine and, therefore, there was probably no increase of intestinal putrefaction. From his study of this case of Lexer, Albu concludes that not more than one-third of the small intestine may be removed without danger to the nutrition, even when that third is computed on the relative length of the intestine to body weight.

Miyaki has reported a case in which 225 cm. of the ileum and 13 cm. of the colon was excised for tubercular ulcers and adhesions. Upon this case Onodera and Jano, two months after the operation, carried out studies in metabolism, which showed a nitrogen excretion of 29.8 per cent, fat elimination of 31.7 per cent, and 0.43 per cent of the diet carbohydrates in the fæces. Although the patient had from one to three stools a day, these observers looked upon this as a practically normal excretion. Seven months later, the patient had only one or two formed stools, and had gained 9.5 kilos in weight. In comparing these figures with other cases, however, particularly in reference to the carbohydrate elimination, it should be remembered that the Japanese diet is particularly rich in carbohydrates.

One of the most extensive resections of the human intestine was made by Nigrisoli, who removed 520 cm. of the small intestine for adhesions and stricture. Vitali studied the metabolism on Nigrisoli's case in a series of observations beginning twenty-two days after the operation, and lasting some twenty-three days. During this period the patient gained some 5 kilos, but Vitali observed, notwithstanding, an increase in the excretion of nitrogen and fats to an extent slightly above normal, as well as an increase in intestinal putrefaction as indicated by the excess of the ethereal sulphates in the urine, thus confirming on man the observations of Erlanger and Hewlett on our dogs. Besides Brugsch, whose work will be described later, Vitali was the only investigator who studied the carbohydrate metabolism in human beings. These substances, like the nitrogen and fat, were also excreted in excess of the normal, a fact, it will be observed, which does not correspond to the metabolic studies on animals with shortened intestines, at least after the compensation has been established.

Zeidler operated upon a young man of twenty, with a large scrotal hernia, in which the contents of the sac had become incarcerated, resulting finally in torsion and gangrene of the intestine. Resection of 318 cm. was necessary. The patient made a good recovery, and two months after the operation, Spassokukozkaja studied the nitrogen metabolism, which he declared was normal. In the abstract, no mention is made of any observations upon the fat or carbohydrate metabolism.

A carefully worked up case of resection of 475 cm. of the small intestine is reported by Axhausen, who removed this large segment of the ileum for vovulus and gangrene in a young woman aged eighteen. This operator measured the remaining portion of the intestine by handspans and estimated about 125 cm. of the jejunum and ileum was left, after the gangrenous portion had been removed. In this case the metabolic changes were studied by Brugsch. As the patient had a tubercular process in each apex, the appetite was poor, and only a moderate amount of food was taken. The diarrhœa was not marked, as there were only two or three soft stools a day, fatty in character and of silver gray color. Microscopically, they showed many fatty acid and soap crystals, undigested muscle fibres, with nuclei and cross striations in good condition. The metabolic observations began sixteen days after operation and showed 36.5 per cent of the diet fat in fæces, of which 25.2 per cent consisted of neutral fats, 24.8 per cent of fatty acids, and 40 per cent of soaps. Of the nitrogen content of the food, 34.2 per cent appeared in the fæces, while the carbohydrates were completely utilized, an interesting confirmation of Professor Underhill's observations on Dogs Nos. 12, 13 and 14. Furthermore, an increase in the amount of ferments in the stools over the normal was observed.

The patient maintained her weight for about three months, but gradually failed, and died of tuberculosis six months after the operation. As Axhausen remarks, her impaired intestinal absorption was probably not without effect on the course of the tubercular process.

Another case of extensive resection of the small intestine is reported by Storp, who excised 510 cm. of the ileum for a sarcoma of the mesentery. There was a slight diarrhœa after the operation, the patient having two or three soft stools a day. Although this was controlled by astringents, it showed a tendency to recur. Notwithstanding, the patient gained in weight, although a microscopic examination of the stools showed more fat and fatty acid crystals than normal. Otherwise, no study was made of the balance between ingestion and elimination in this case. A short time later multiple metastases were found in various parts of the body, and the patient was discharged without further treatment, owing to the hopelessness of the condition.

Denk reported the two cases of extensive resection of the ileum operated on by Brenner of Linz. The first was a case of intussusception from a polyp, for which 250 cm. was removed. The patient showed no digestive disturbances. The second case is the largest reported resection in the literature, where Brenner removed 540 cm. of the ileum in a woman aged sixty-one, for gangrene, due to torsion of the intestine in a large femoral hernia. The patient made an excellent recovery, and showed but little disturbance of her metabolism. She had about five fluid stools a day, which were bad-smelling, and contained much undigested food. Later, conditions improved,

and Denk made a test of the functional efficiency of the intestine by Schmidt's method, which indicated a normal digestion. About one and one-half years after the operation, Denk repeated the test. At this time she had from three to four soft or fluid stools a day, the latter condition occurring particularly after taking much coffee or milk. Although there was a diminished fat absorption, the patient maintained her weight and was able to do her housework without fatigue. Otherwise, the metabolism was perfectly normal.

A subsequent report on this case made by Denk recently shows the importance of a guarded prognosis even in apparently successful cases of extensive resection of the small intestine. A year after the last report was published, or 2½ years after the operation, the patient died of marasmus. At the time of operation, the patient weighed 48 kilos, and just before death, 26½ kilos. There was a general atrophy of all the organs, particularly of the omentum, confirming in main, the conditions found in some of our experimental animals (Fig. 1). No compensatory hypertrophy of the intestine was found in the case.

My own second case, which is reported in detail later in this paper, was studied metabolically by Underhill, who found that the infant of 11 months of age, showed during the period of severe diarrhœa 10 days after the operation, an increase in the fat excretion and an incomplete utilization of the carbohydrates, as a test for lactose was obtained. In the second series of experiments, made five weeks after the operation, after compensation was established, the fat excretion had dropped from 20 per cent to 9 per cent, and no test for lactose was present, although carbohydrates were excreted to the extent of 5 per cent, due to the presence of an indigestible cereal in the food.

The results of the metabolic studies on the human cases may be tabulated as follows:

Investigator	Case	Resection	Per cent of diet N. in fæces	Per cent of diet fat in fæces	Per cent of diet carbohydrate in fæces	Intestinal putrefaction
Underhill.....	Flint's.....	100	15	21	1	No obs.
Underhill*.....	Flint's.....	100	16	8	4	No obs.
Plaut..... ..	Schlatter's.	192	10.47	13.91	No obs.	No obs.
Albu.....	Lexer's....	200	10.12	10.1	No obs.	Not increased
Onodera & Jano....	Miyaki's. ..	238.5	29.8	31.7	0.43	No obs.
Riva-Rocci.....	Fantino's..	310	29.0	23.0	No obs.	No obs.
Zusch	Barth's.....	316	13.7-21.3	18.1-38.5	0.51-0.61	No obs.
Spassokukozkaja ..	Zeidler's...	318	Normal	No obs.	No obs.	No obs.
Sagini.....	Ruggi's.....	330	9.5	13.7	No obs.	No obs.
Brugsch	Axhausen's	475	34.2	36.5	0	No obs.
Vitali.....	Nigrosoli's.	520	Incr'sed	Incr'sed	Incr'sed	Incr'sed
Denk.....	Brenner's..	540	Normal	Incr'sed	Trace	Not increased

* Second period.

An inspection of this table containing the observations on those cases of extensive resection of the small intestine in man where the metabolic changes were studied, confirms, in general, the findings upon the metabolic processes in dogs with shortened intestines. There is no constant ratio between the length of the resected portion of the ileum and the degree to which the absorption of nitrogenous and fatty substances is diminished. The difficulty in harmonizing these results is due, no doubt, to the differences in the diets on which the patients were tested, and to a number of unknown factors, such as the exact length of intestine left at operation, or, in other words, the variability of the intestine, difficulties of measurements, resistance and condition of the patient, not to speak of the known variations of age, pathological conditions, etc. In general, however, the results of these observations are in accord with those upon animals. Moreover, the subsequent history of Schlatter's case, as told in his letter to Albu, indicates that the same gradual improvement observed in dogs also takes place in man. As in the observations in dogs, the increased intestinal putrefaction is undoubtedly due to the food remaining for a longer period than normal in the large intestine.

TABLE OF CASES OF RESECTION OF SMALL INTESTINE EXCEEDING 200 CM.

No.	Operator and publication	Amount resected cm.	Result	Metabolic disturbances	Remarks
1	Flint: Johns Hopkins Hosp. Bull., 1912, xxiii, 133.	Ileum, 100 Colon, 18	Recovery	Severe	Intussusception and gangrene. Infant 11 months old.
2	Lexer Berl. klin. Wchnschr., 1900, xxxvii, 4.	200	Recovery	Moderate	Fibroma of mesentery.
3	Peterson: Ref. Ruschhaupt, Inaug. Diss., Bonn, 1901.	202	Recovery	None	Prolapse of intestine. Stab wound of abdomen.
4	Flint: Johns Hopkins Hosp. Bull., 1912. xxiii, 135.	Ileum, 204 Colon, 55	Death	Violent	Colloid carcinoma of transverse colon and intestinal adhesions.
5	Koeberlé: Gaz. hebd. de méd., 1881, 2. s., xviii, 55.	205	Recovery	None	Stricture.
6	Miyake: Arch. f. klin. Chir., 1910, xciii, 768.	206	Death	....	Adhesions to ovarian tumor. Death. Peritonitis.
7	Enderlen: Ref. Lauenstein. Deutsche Ztschr. f. Chir., 1909, c, 169.	207	Recovery	....	Strangulated hernia.
8	Kocher: Ref. Trzebicky, from letter.	208	Recovery	Slight	Rupture of intestine.
9	Dreesman: Berl. klin. Wchnschr., 1899. xxxvi, 837.	215	Recovery	Moderate	Gangrene, incarcerated hernia.
10	Mikulicz: Rothe, Beiträge z. klin. Chir., 1902, xxxiii, 140.	215	Recovery	None	Gangrene. Hernia.
11	Karlow: Hygiea, 1903, f iii, pt. 2, 460.	215	Recovery	None	Gangrene, omental bands.
12	Axhausen: *cide inf.*	215	Recovery	....	Tubercular stricture of intestine.
13	Dekonski: Ref. Istomin, Russ. med. Rundschau, 1910, viii, 329.	220	Recovery	....	....
14	Thon: Deutsche med. Wchnschr., 1909, xxxv, 742.	220	Recovery	....	Ileus.
15	Kouwer: Nederl. Tijdschr. v. Geneesk., Amst., 1898, 2, ii., xxxiv, d 2, 887.	224	Recovery	None	Gangrene, hernia.
16	Miyake: Loc. cit.	Ileum, 225.5 Colon, 13	Recovery	Slight	Tubercular ulcers and adhesions. Two to three soft stools *per diem*.
17	Monprofit: Rev. de Chir., 1899, xx, 579.	Ileum, 230 Colon, 80	Recovery	Slight	Adhesions, hernia.
18	Shepard Centralbl. f. Chir., 1898, xxv, 397.	237	Recovery	Slight	Tumor mesentery.
19	Kukula: Arch. f. klin. Chir., lx, 877.	237	Recovery	None	Tumor mesentery. Recurrence 1½ yrs. later. Death.
20	Harris: Med. Rec., N. Y., 1902, lxii, 563.	239	Recovery	Slight	Gangrene, hernia.
21	Hayes: Blayney, Brit. M. J., 1901, i, 399.	248	Recovery	Slight	Rupture of mesentery.
22	Brenner: Denk. Wien. klin. Wchnschr., 1907, xx, 1649.	250	Recovery	None	Intussusception from polyp.
23	Enochin: Ref. Istomin (see Dekonski).	250	Recovery	....	.....
24	Peck: Ref. Harris.	251	Recovery	....	Rupture of uterus.
25	Lauwers: J. d. Chir., et Ann. Soc. belge de Chir., 1901-2, i, 739.	265	Recovery	....	Gangrene hernia.
26	Park: Arch. internat. de Chir., 1904, i, Fasc. 1.	265	Recovery	....	Gangrene following appendicitis.

TABLE OF CASES OF RESECTION OF SMALL INTESTINE EXCEEDING 200 CM.—*Continued.*

No.	Operator and publication	Amount resected cm.	Result	Metabolic disturbances	Remarks
27	Pokotilo: Chirurgia, 1908, xxv, 109.	270	Recovery	....	Strangulated hernia.
28	Mitchell: Ref. Kelly-Noble Abdominal Surg'y, Phila., 1908, p. 442.	274	Death	....	Thrombosis of mesenteric artery.
29	Payr: Arch. f. klin. Chir., 1902, lxvii, 181.	275	Recovery	None	Gangrene.
30	Kopfstein: Revue d. Böhm. Med., 1909. Ref. Wien. med. Bl., 1910.	275	Recovery	Slight	Tubercular stricture of intestine.
31	Maymdl: Ref. Kukula.	284	Death	Inanition	Carcinoma of cæcum. Death in 21 days.
32	Childe: Brit. M. J., 1907, ii, 891. Practitioner, 1909, lxxxii, 364.	289	Death	Inanition	Gangrene, hernia. Died 7 months after operation, from inanition.
33	Lorenz: Wien. klin. Wchnschr., 1906, xix, 610.	292	Recovery	....	.....
34	Göbell: Deutsche Ztschr. f. Chir., 1905, lxxvii, 608.	300	Recovery	Slight	Mesenteric hernia and volvulus.
35	Friedrich: Med. Klin., 1904-5, i, 25.	300	Recovery	....	Septic peritonitis, short-circuiting without resection.
36	Fantino: Riforma med., 1902, xviii, pt 4, 736, 748, 758.	300	Death	Inanition	Adhesions to fibroma uteri. Death one month later.
37	Fantino: Gazz. med. di Torino, 1896, xlvii, 181.	310	Recovery	Moderate	Gangrene, volvulus.
38	Ghedini: Clin. Chir., Milano, 1905, xiii, 278.	315	Recovery	....	Strangulated hernia. Death in 3½ mos. Marasmus.
39	Barth: Deutsche med. Wchnschr., 1909, xxxv, 509.	316	Recovery	Slight	Ovarian tumor, fecal fistula, short-circuiting, later resection of short-circuited loop.
40	Fischer: Ref. Centralbl. f. d. Grenzgeb. d. Med. u. Chir., 1903, ix, 70.	316	Recovery	....	Incarcerated hernia.
41	Zeidler: Spassoku kozkaja, Russk. Vrack., 1906. Ref. Centralbl. f. Chir., 1906.	318	Recovery	....	Hernia.
42	Whitall: Ann. Surg., 1911, liv, 669.	320	Recovery	None	Abortion. Perforation of uterus.
43	Morton: Ref. Kelly Noble Abdominal Surg'y, Phila., 1908, p. 442.	322	Recovery	....	Myxosarcoma of mesentery.
44	Ruggi: Centralbl. f. Chir., 1896, xxiii, 365.	330	Recovery	....	Strangulation and adhesion. Three operations.
45	Staehlin: Ann. Surg., 1907, 45, 49.	335	Recovery	Slight	Strangulated hernia. Recovered perfectly.
46	von Eiselsberg: Ref. Park.	350	Death	Inanition	Lived 25 days.
47	Baracz: Arch. f. klin. Chir., 1907, lxxxiii, 478.	350	Death	....	Strangulated hernia gangrene; lived 2 days.
48	Nicola: Clin. chir., 1910.	350	Recovery	....	Incarcerated umbilical hernia.
49	Werelius: J. Am. M. Ass., 1907, xlviii, 945.	365	Recovery	Slight	Abortion, rupture of uterus.
50	Obalinski: Arch. f. klin. Chir., 1894, xlviii, 16.	Ileum, Cæcum, 365	Death	....	Gangrene, hernia; died in 22 hours
51	Mitchell: Brit. M. J., 1902, ii, 975.	366	Recovery	....	.....
52	Pauchet: Ref. Gazz. d. hôp., 1905, 1667.	400	Recovery	Violent	Gangrene, hernia.
53	Friedrich: Med. Klin. 1904-05, i, 25.	400	Recovery	....	Functional short circuit.
54	Axhausen: Mitth. a. d. Grenzgeb. d. Med. u. Chir., 1909, xxi, 55.	475	Recovery	Moderate	Volvulus, death 6 months later, tuberculosis.
55	Stolz: Deutsche med. Wchnschr., 1909, xxxv, 744.	475	Recovery	Slight	Fatigue after exertion.
56	Storp: Deutsche Ztschr. f. Chir., 1907, lxxxvii, 313.	510	Recovery	Moderate	Sarcoma of mesentery; recurrence, death.
57	Nigrisoli: Jahresbe. f. Chir., 1902, viii, 754.	520	Recovery	Moderate	Obstruction from adhesions.
58	Ghedini: Loc. cit.	524	Recovery	Slight	Strangulated hernia. Short-circuited.
59	Brenner: Denk, Wien. klin. Wchnschr., 1907, xx, 1649.	540	Death	Slight inanition	Gangrene, hernia. Died of marasmus 2½ years after operation.

In addition to the cases on which metabolism experiments were conducted, there are many others in the literature where large amounts of the small intestine have been resected. Some of these have shown digestive disturbances and others not. As I have succeeded in finding fifty-eight instances, including the cases reported in this paper, where 200 cm., or more of the intestine have been removed, a list of the cases is given above, together with the chief points of interest in the history.

In consideration of this series of cases, several facts should be borne in mind. In the first place, in the measurement of an extremely elastic organ like the intestine, there has been no standard to guide the investigators who have reported the various cases. Great errors are thus unconsciously liable to exist. Furthermore, there may be extreme differences in measurement, due to the viability of the gut. Living intestine, exposed to the air, will, owing to contraction of the longitudinal muscle, shrink to less than half its normal length. Dead or gangrenous gut, on the other hand, after losing its tonicity may measure much more than its normal. Another point of importance which should not be overlooked, is that successful resections of large portions of the intestine are much more likely to be reported than unsuccessful attempts, giving us, in all probability, much too low a mortality.

The history of my cases is as follows:

CASE I.—W. J., male, aged twenty-nine, American, conductor. Admitted November 9, complaining of pain in the abdomen.

Present Illness.—Began one month ago with a generalized pain over the whole abdomen, paroxysmal in character, lasting from a few minutes to an hour. They occurred twice or three times a week and were associated with constipation. Bowels were moved with the aid of cathartics and enemas. Three days before admission, the patient was seized with an attack of pain similar in character, but much severer than his previous seizures. The pain eased somewhat the next morning, but there were frequent attacks during the day. These gradually increased in frequency until on the day of admission they occurred every few minutes. The pain is generalized, does not radiate to the back, shoulder, or any part of the abdomen or extremities. On the day of admission, patient vomited several times. Vomitus was greenish in color and of a sour odor. Bowels moved last before the beginning of the present attack, although on the night before admission, after taking an enema of warm water, the patient passed a few hard lumps of fæces. There has been no loss of weight. Appetite has remained good, and bowels have been regular until the onset of his present illness. At no time has he passed blood with his stools.

Past History.—In 1900, patient was thrown from his horse and apparently recovered. A few weeks later, while on a train en route to California, he was taken sick suddenly, became unconscious, and was carried to San Francisco, where he was operated upon. He was told that he had broken a blood vessel in his back, which was tied after a large clot was removed. He related, rather with pride, that he had torn open his wound on the day after the operation. He was very sick, and recovered only after a prolonged convalescence. His appendix was not removed at this operation. The wound was, from his description, drained for some time.

Family History.—Negative.

Physical Examination.—Negative, except for abdomen. Abdomen slightly distended. There is an irregular scar 6 cm. long, 3 cm. outside the linea semilunaris, midway between the anterior superior spine and the costal margin. The cicatrix has the

appearance of resulting from a suppurating wound. There is a slight fullness between the scar and umbilicus. Abdomen otherwise symmetrical. Respiratory movements present. No visible peristalsis or tumor masses. Panniculus poorly developed, so that abdominal musculature stands out clearly. Flanks symmetrical. Liver dullness extends from upper border of seventh rib to a point 3 cm. above costal margin. Edge of liver not felt. Stomach tympany not increased. During examination there are numerous attacks of pain, during which the knees are promptly flexed, but no peristalsis is visible. There is general abdominal rigidity, the right side being more tense than the left. Between the attacks the abdomen is softer, but no masses are palpable. No constant muscle spasm; deep palpation sometimes elicits spasm, and at other times not. No particular tenderness over appendix, gall bladder, or sigmoid. Pain seems generalized. Percussion much more painful than palpation. Abdomen everywhere tympanitic, except in the flanks, where the note is somewhat flat. No movable dullness.

Rectal Examination.—Prostate of normal size and consistency; not tender. Cul de sac filled with distended intestines. No inflammatory masses felt. Neither side tender to touch.

No hernia of linea alba. No inguinal, femoral, umbilical, perineal, or sacral hernia. No hernia in Petit's triangle.

Genitalia negative. No nodules on tibia. Reflexes normal.

Leucocytes 10,200. Temperature 99.4° F.; pulse 80, respiration 28.

Urine shows nothing abnormal.

From the history of the case, the possibility of neoplasm was thought of, although owing to his age it seemed more probable that he was suffering from a partial obstruction due to adhesions resulting from previous operations, although they had not given him the slightest trouble until the onset of the present illness.

A rectal tube was passed and a high enema of hot oil was given. Some gas and a little fæcal material was passed. An hour later a stomach tube was passed full length, and the enema repeated and a small movement obtained. There was no blood, and the fæces were well mixed with oil.

November 10. Patient has had two spontaneous movements, and is resting quite comfortably. An exploration was advised while the patient was in good condition, and accepted.

November 11. *Operation.*—Median incision at the level of the umbilicus. The ileum in the entire right upper quadrant was found matted together by firm, well-organized adhesions, which also bound it to the abdominal wall in the neighborhood of the old scar. The ascending and first part of transverse colon could not be reached owing to the adhesions. Cæcum was free and appendix normal. To facilitate the liberation of the adhesions, the old cicatrix was excised and the peritoneum opened midway between the hepatic flexure and cæcum. The ileum was carefully dissected free from the abdominal wall, and adjacent adherent loops liberated. In many places the union was so intimate that the muscle coat of one loop was injured, and once a small hole was torn in the bowel. This was immediately closed with a purse string suture, reinforced with several mattress sutures. Approximately seven feet of small intestine were involved in this mass of adhesions. Several stenoses and loops matted togethed in U shapes were found. As soon as the colon was uncovered, further palpation revealed a tumor mass in the transverse colon, just distal to the hepatic flexure. The tumor had a sharp constriction in the center, suggestive of an annular carcinoma. Adhesions made the palpation of the glands in the mesocolon uncertain. For fear of a recurrence of the adhesions in the small intestine, or necrosis of the intestinal wall where the muscular tunic had been injured, it was decided to resect the entire lower seven feet of ileum, together with the cæcum, ascending colon, and half of the transverse colon. A well-nourished point of healthy ileum was selected and the end invaginated, as in the treatment of the appendix stump. The mesenteric vessels were caught between clamps and divided, where possible, and ligated with fine silk by transfixion. The division and ligation of the branches of the superior mesenteric, ileocolic, colica dextra, and colica media to the middle of the transverse colon followed, although this stage of operation was rendered difficult by the presence of chronic enlarged glands, which were probably a residue of the old peritonitis. The cæcum and ascending colon were then freed by incision of the lateral reflexion of the mesocolon.

Finally, the gastrocolic omentum was incised, bleeding points ligated, and the transverse colon freed from the stomach up to the point selected for the anastomosis. Here the colon was divided, cauterized, and invaginated, as in the treatment of the appendix stump. The lower end of the ileum was then laid beside the transverse colon and a lateral ileocolostomy performed by means of the intestinal scissors, which I have described in another paper. The anastomosis was accomplished without a leak. The cut edge of the mesentery of the small intestine was held to the cut edge of the transverse mesocolon by the anastomosis. Sutures were unnecessary, owing to the overlapping. It was impossible to cover the peritoneal defect left by the ascending colon with the peritoneum and ascending mesocolon, owing to the inelasticity of the peritoneum, due to the old adhesions. The median wound was closed in layers, and the site of the original wound by through and through silkworm gut. A cigarette drain was passed from this wound down to the denuded area.

The resected portion of the small intestine measured 204 cm. collapsed, and 215 cm. distended. The firm adhesions prevented the usual great lengthening of the intestine when distended with fluid, as is usual in such cases. The resected portion of the colon measured 55 cm. On microscopic examination, the tumor proved to be a colloid carcinoma of the transverse colon, with metastases already present in the peripheral lymph spaces of the glands in the adjacent mesocolon.

The patient recovered from the ether rapidly, but was restless and complained of a great deal of pain. After morphine he seemed more comfortable. Maximum temperature 99.6° F., pulse 100, respiration 28.

November 12. Patient complains of severe pain, which morphine does not seem to control. There has been continuous proctoclysis since the operation. This fluid consisted of 15 per cent glucose in normal saline. The glucose was boiled and rendered alkaline. We felt it desirable to give the patient some nourishment, if possible, from the time of operation. Very restless, and tosses to and fro in bed a great deal. Temperature 98.4°-100.8°F., pulse 90-100, respiration 20.

November 13. Patient still complains of considerable pain in abdomen. Abdomen soft and not distended. Proctoclysis continued. Albumen water started and well borne, as the patient was suffering from thirst. During the evening the bowels moved spontaneously. Small dark fluid stool. No blood. Temperature 98.4°-99.2° F., pulse 80-95, respiration 20.

November 14. Patient feels well this morning, but is still somewhat restless. No change was observed until this afternoon, when, while the nurse's back was turned, patient jumped out of bed and rushed to the window. Broke a pane of glass trying to climb out. Afterwards seemed somewhat irrational. This evening asked for whiskey and cigarettes. There are no signs of an alcoholic psychosis, although patient gives a history of being a heavy periodic drinker. During the day patient had eight movements. Temperature 97°-99.8° F., pulse 76-90, respiration 20.

November 15. Patient passed a very restless night. Still very restless; complains of pain, but in no particular spot. Abdomen soft and not distended. Morphine and codein do not seem to control him. Diarrhœa continues. Movements becoming more frequent. Patient is given soft carbohydrate diet. At 1 o'clock he was given 8 ccm. of paraldehyde on the assumption that his postoperative psychosis might have some relation to his deprivation of alcohol. He immediately vomited violently and complained of

sharp pain in the epigastrium. His pulse rose rapidly from 80, at the time he vomited, to 120 at 8 P. M. At this time his temperature was 99.8° F., and respiration 25. Diarrhœa, twenty movements, some of which are voluntary.

November 16. Patient much worse this morning. Pulse remains high, temperature subnormal. Abdomen distended in both upper quadrants. Patient complains of great pain, chiefly in upper abdomen. Marked Hippocratic facies. Diarrhœa more marked, twenty-two movements, many involuntary; no blood. Dressing showed that the continual movements of the patient caused the sutures to cut partially through. Wound reddened, and some pus found around the drain. Median incision looks well. Temperature 96°-98.4° F., pulse 100-138, respiration 20-30.

November 17. Patient much worse. Temperature remains subnormal, pulse high. Toward noon he was almost moribund, and died at 7.30 P. M.

Permission could not be obtained for a complete autopsy, but consent was given to reopen the wound.

The median wound was healing superficially, but there was a small pocket of pus in the subcutaneous tissue about one of the catgut sutures. Omentum adherent to the line of incision. General peritoneal cavity free, peritoneum glistening and of good color. Anastomosis in good condition. No leak and very little reaction about it. A loop of ileum was found driven up between the left lobe of the liver and diaphragm. The loop is kinked, but there is not complete obstruction. It is covered with a fresh, heavy, fibrous exudate, which can be picked off, and shows two or three fairly large areas of beginning gangrene. On the right side of the peritoneal cavity, corresponding to the denuded area left by the ascending colon, is a walled-off area of local peritonitis into which the drain projects. There is some pus in this region. Probably the infection had travelled down the drain from the broken-down skin wound. There was no evidence of any compensatory process in the remaining portion of the intestine, for the removal of the segment of ileum and colon.

Remarks.—We could not account for the psychosis shown by the patient after the operation. It will be remembered that he behaved in a similar fashion after his operation in San Francisco. On the whole, he suffered remarkably little discomfort in the first three days after the operation, considering the nature and magnitude of the procedure. Save for his restlessness and continued motion, he was in excellent condition until the vomiting spell after the administration of the paraldehyde. It was undoubtedly at this time that the loop of the ileum was incarcerated between the upper surface of the left lobe of the liver and diaphragm. This was indicated by the prompt change in his vital signs, although there was no complete obstruction, as was shown by the continuation of the diarrhœa. The distension in both upper quadrants the next morning is evidence that there was partial obstruction above the incarcerated loop.

Of special moment, at this time, is the fulminating diarrhœa which was inaugurated about fifty-two hours after the operation, and continued with increasing severity until the patient died. The stools were fluid, small in quantity, foul-smelling, but contained no blood. While in no way immediately responsible for the patient's death, the debilitating effect of the diarrhœa undoubtedly had an influence on his resistance and vitality. From the resection of the ileum, or the colon alone, no such violent reaction could have been anticipated. Indeed, in view of Monprofit's case, even the reaction to the combined resection seems excessive, although it must be remembered of Mayndl's case, where a less extensive resection of the colon was done, the patient died of inanition.

It may not be out of place here to recall Cannon's interesting work on the movements of the colon, in course of which he found that the waves, up to a point about the beginning of the descending colon, were predominatingly antiperistaltic, while in the remainder of the large intestine the peristalsis was directed towards the rectum. These results are confirmed by the observations made on human beings by means of the X-rays after the ingestion of bismuth meals. Under ordinary circumstances, the contents of the stomach are found in the cæcum, about five or six hours after the meal is taken. Then they are found chiefly in the cæcum, ascending colon, and transverse colon, until about twenty-three hours after the meal, when they are deposited in the rectum. It will be seen, then, that we removed not only 204 cm. of the lower end of the ileum, but practically all of that portion of the colon where the intestinal contents remain longest.

In cases reported by the Mayos, where similar segments of the colon have been removed, no mention is made of a subsequent history of violent diarrhœa, and particularly Arbuthnot Lane's series of resection of the entire colon have shown, according to Lane, a violent post-operative vomiting as the single serious consequence of the operation. Harley's studies on the metabolism of dogs, from which the large intestine had been removed, reveal few disturbances of the equilibrium between intake and excretion, except in an increase in the elimination of water. Fat absorption is unaffected, while the observation on the nitrogen elimination varies; in one animal it is increased, and in another remains unaffected. Simple short-circuiting operations teach us nothing in respect to the conditions we are dealing with, as the intestinal contents in these operations tend to follow the usual course which the food takes. Even an anastomosis of the ileum with the sigmoid, where a complete stenosis exists, might still allow the food delivered into the colon to be carried back into the cæcum by antiperistalsis.

Fantino, after the death of his patient from inanition due to the resection of 300 cm. of ileum, drawing conclusions from another patient on whom, owing to error, he had created a sort of vicious circle while short-circuiting the entire colon and about 100 cm. of ileum, by reversing the anastomosis, suggests this as a regular procedure in cases of extensive resections of the intestine, because his patient stood the operation so well. He believes that, in this way, we might keep the intestinal contents long enough in the remaining segment of gut to allow the completion of the digestive processes.

CASE II.—The second case is included in this series, notwithstanding the fact that only 100 cm. of the ileum was resected, but owing to the fact that the small intestine in infants of this age is only nine feet, the resection of 100 cm. is equivalent to the arbitrary limit of 200 cm. taken in adults.

A. K., aged 11 months, male. Admitted December 14, 1910; the mother states that the child is suffering from stomach and bowel trouble.

Present Illness.—For about 4 months the child has been suffering from a mucous entercolitis. The condition has apparently become progressively worse up to the present time. About one month ago the child was taken from the breast and given artificial feeding. Vomits occasionally. Has given evidence of frequent colicky pains. This afternoon, without any particular increase in the severity of the symptoms, the child had a stool mixed with blood and mucus. It was on this account the infant was brought to the hospital.

Past History.—No previous illness; normal delivery; weight at birth 10 pounds.

Physical Examination.—Patient is a fairly well developed baby, weighing 16 lbs., 14 ozs., somewhat anæmic in appearance; sits up well. Has a distinctly anxious expression, but gives no evidence of acute pain; climbs around on the bed during examination. No enlargement of cervical glands. Anterior fontanelle nearly closed. Heart and lungs negative. Abdomen slightly distended. No visible peristalsis or tumor masses. Abdomen perfectly soft. No general abdominal rigidity. Liver dullness not increased. Palpation of upper abdomen negative. No masses felt in the right iliac fossa. Extending up out of the pelvis toward the left iliac fossa, in the region of the sigmoid, is a small rounded tumor, not long enough to be definitely sausage-shaped. Tumor is apparently not tender, but palpation is followed by the appearance of an intestinal pattern with visible peristalsis. No moveable dullness. During the examination a muco-hemorrhagic stool of about 20 cc. was passed. Rectal examination revealed a tumor very much like an elongated cervix. The lumen at the apex of the intussusceptum felt exactly like the external os, and the finger could be freely passed between the intussusceptens and the intussusceptum. Straining followed the digital examination, resulting in the prolapse of about 8 cm. of the intussusceptum. Temperature 99.8° F., pulse 100, respiration 28. Urine showed trace of albumen and occasional hyaline casts. Immediate operation for the obvious condition of intussusception was advised and accepted.

Operation.—Median incision 15 cm. long, extending both above and below the umbilicus. The exploration showed the invagination of almost the entire lower half of the ileum, cæcum and colon into the sigmoid. The intussusception could be reduced to a point at about the middle of the transverse colon, when gangrenous intestine began to appear. In order to obtain a healthy intestine for anastomosis, it was necessary to resect 100 cc. of the ileum, cæcum, ascending colon, and one-half of the transverse colon. Owing to the collapse of the patient as soon as the abdomen was opened, anæsthesia was suspended, and the operation continued hurriedly without any further administration of ether until the incision was closed. The mesenteric vessels and mesocolon were ligated by transfixion, and the intestine freed to the point of anastomosis. Owing to the distension of the small intestine, an end-to-end anastomosis, by means of the Murphy button, was easily accomplished, and the defect in the mesentery and mesocolon was sutured together and the abdomen closed without drainage.

Examination of the specimen showed that the apex of the intussusceptum, projecting from the anus, was formed by the ileum at a point about 70 cm. above the ileo-cœcal valve, and the intussusception was one of the ileo-cœcal variety. Measurement of the specimen after the operation showed that 100 cm. of ileum and approximately 18 cm. of colon had been resected.

December 15. Temperature has risen to 101.6° F., pulse 160, and respiration 30, since the operation. Six muco-hemorrhagic stools were passed. Child appears to be in fairly good condition.

December 20. Condition of the patient has been serious since the operation. Pulse has averaged about 130. Axillary temperature between 98.4° and 100° F. There have been from eight to nine muco-hemorrhagic stools a day. Child took very little nourishment, other than a small amount of milk the first four days after the operation. Drank copiously of water. A rectal drip of 10 per cent dextrose in normal saline was maintained for four days after the operation. Abdomen has been soft. Blood ceased to appear in the stools on the fourth day, but they remain mucous in character. Murphy button was passed this morning.

December 26. Rectal temperature has ranged from 100°-98° F.; pulse has dropped to between 100-120; respirations from 20 to 24, there now being on the average of 10 stools a day, with occasional streaks of blood. For the last three days the urine and fæces were collected and metabolism studied by my colleague, Prof. Underhill, to whom I am indebted for the figures presented. During this period the balance of intake and output is shown in the table at the end of the history. The diet during this period has been peptonized milk, 4 ounces every two hours, some of which was refused.

December 29. Weight, 15 lbs. 8 ozs. Child appears to be improving. Now takes about 1 pint, 10 ozs. of milk per day.

January 1, 1911. Vital signs have been practically normal for the last five days; all stitches removed and wound healed per primam.

January 4. Weight, 16 lbs. Stools average 6 to 7 a day, occasionally mucous in character.

January 10. Weight, 16 lbs. 8 ozs. Six stools per day. No blood since last note.

January 23. Weight, 17 lbs. 10 ozs. Averge 3 to 4 stools per day. No mucus.

January 28. Weight, 17 lbs. 14 ozs. Three good stools a day; no mucus. Discharged from the hospital.

On the 25th and 26th, a second series of metabolic studies were undertaken. The results with the former test are shown in the following table:

Dates	Per cent of diet N. in fæces	Per cent of diet fat in fæces	Per cent of diet carbohydrates in fæces	Test for lactose	Positive balance grams N. retained per diem
December 24, 25, 26...	15	21	1%	Positive	+2.70
January 25.....	16	8	4%*	Negative	+0.49
January 26	22	9	5%*	Negative	+0.35

* The cereal was passed in the stool in undigested form.

The diet has been increasing to about a pint of full milk a day, with a small amount of Cream of Wheat (breakfast cereal) or toast. The study of this table shows that, while the nitrogen elimination has increased slightly, the fat elimination is markedly decreased. The percentage of carbohydrates in the fæces in the second series of experiments appears normally high, but this fact is due to the passage of the cereal in an undigested form. Of great importance is the fact that, while a test for lactose was obtained at the first examination, during which the child was suffering from diarrhœa, there was no trace of it either January 25 or January 26 after compensation was established. The course of the case is somewhat complicated by the existing enterocolitis, before the appearance of the intussusception. As the number of stools had been but three or four a day before the operation, the increase is undoubtedly due, as in the animals we operated upon, to the shortening of the small intestine. Notwithstanding the loss of one-third of the ileum, together with a large portion of the colon, the child was able to neutralize the loss,

and showed a consistent gain in body weight, and a constant improvement in the condition of the intestinal irritability. The weight increase is shown in the positive balance by the retention of 0.49 and 0.35 grams of nitrogen in the two days of the second period. The retention of 2.70 grams per day during the first period, ten days after the operation, apparently indicates the desperate effort the child was making to maintain its weight during the most active period of the diarrhœa. At this time, the general nitrogen elimination was somewhat lower than during the second period, but the fat excretion was much higher. Unfortunately, we have no data from normal cases to compare with the conditions shown by this child. The absorption of the lactose reaffirms the observations made on animals, and other human patients, and indicates the value of such readily absorbable carbohydrates, as the simple sugars, in the diet of these cases as well as the importance of employing them for nutritive enemata, as was done in both of our cases.

In this series of fifty-eight cases there were nine deaths, giving a mortality of a little over 16 per cent. While most deaths from the resection occurred where 274 cm. or more were removed, nevertheless 510, 520, and 540 cm. have been successfully taken out. In a variety of pathological conditions involving the small intestine, it would appear that the removal of portions of the ileum measuring 275 cm. is relatively safe. Schlatter's case, where only 192 cm. were resected, Dreesman's, where the amount removed was only 215 cm., and my own, gave much severer metabolic disturbances than the cases of Storp, Nigrisoli, and Brenner, the maximum successful resections in the literature. It is, then, natural to seek the explanation of these differences, partially in errors in measuring the length of the resected portion of the gut, but more probably in such accessory and important factors as the age, the condition of the patient, the total length of the intestine, and the effect of the pathological condition upon the patient's strength and resistance. Obviously, the result of the operation depends upon these features of the case as well as the length of the resected segment.

The clinical manifestation of the metabolic disturbances caused by an abbreviation of the intestine consist largely in a diarrhœa which, in the majority of instances reported, was only slight in degree, the patient ordinarily having two or three soft or fluid movements a day. These stools were often fatty in character, indicating the inability of the patient to absorb the fatty content of the food. In other cases, the disturbances were moderate in degree and, in still others, like the cases of Pauchet and myself, the diarrhœa was of a fulminating character. Another type of reaction to the removal of the gut was shown where the patients recovered from the operation, but suffered from such profound limitation of the power of absorption that they died later of inanition. The cases of Mayndl, von Eiselsberg, and Fantino were examples of this type, all of which lived about a month after the resection of the intestine. Brenner's case, first reported as successful, finally died of inanition 2½ years after the operation.

Morphological Changes Following the Operation.

In several cases, experimental investigations upon resection of the small intestine have been carried out during the past fifteen years. The first of these were the researches of Senn, whose paper, unfortunately, was not available to me. He gives the limit of resection as 33 per cent of the small intestine. To remove more than this amount is a dangerous operation that will result in marasmus, and terminate sooner or later in death. Senn, according to the authors who have quoted him, also described a compensatory hypertrophy following the removal of the gut. Later, Trzebicky undertook to establish, by means of experiment on animals, the limit of resection of the small intestine. He removed, in a series of dogs, 25, 50, 75, 100, 150 and 200 cm. of the combined jejunum and ileum. In one series, he removed the upper, in another, the middle and in a third, the lower portion of the gut. Trzebicky judged the metabolic disturbances from the post-operative loss of weight in his animals. His results led him to conclude that only 50 per cent of the combined ileum and jejunum could be removed without serious metabolic disturbances, and that the excision of 75 per cent led to such profound changes in the digestive apparatus that life was impossible. At the autopsies on his animals, he found, when large percentages had been removed, a dilatation of the intestines and a disappearance of fat. A compensatory hypertrophy could not be found by this author. In applying his results to the human intestine, Trzebicky stated that not more than 280 cm. should be excised, as the total length of the combined ileum and jejunum in man was, according to his measurements, from 561 to 870 cm. He found, furthermore, that the removal of the jejunal end of the intestine led to more profound losses in weight than when the lower end of the gut was resected.

Monari, in 1896, by a series of operations on dogs, endeavored to establish the limits of resection in the gastro-intestinal tract. He removed the entire stomach of a dog and found no interference with the metabolism. Then he took a series of five dogs from which he removed 186, 170, 249, 215 and 200 cm. of the small intestine respectively. The operation, in spite of a rich diet, was followed by a period of denutrition, which was characterized by profuse diarrhœa, followed by improvement with frequent relapses. The dogs from which 186 and 200 cm. had been removed died within three months. The autopsy showed great loss of weight, atrophy of the muscles, absence of fat and anæmia. In the first dog there was 15 cm., and in the second there were 12 cm. of intestine, exclusive of the duodenum, remaining. The other three dogs lived eighteen months, but never regained the weight they lost after the operation. They had respectively 19, 16 and 20 cm. of small intestine remaining.

From the microscopical examination of the specimens obtained from these dogs, Monari states that the mucous membrane was twice the thickness of the control animal. The villi were more numerous and larger, and the cylindrical epithelium, with which they are clothed, showed an increase in the number of goblet cells, which at the base of the villus

are larger and more numerous than in the norm. The lymph follicles are enlarged, and likewise the circular layer of muscle, while the longitudinal coat showed no change. De Filippi, whose results were published separately, studied the changed metabolism in the dog from which 190 cm. of intestine had been removed, and found no changes, except in a diminished fat absorption. From his work Monari believes that 50 per cent of the human intestine can be removed without the danger of metabolic disturbances.

A most interesting recent contribution to the study of extensive intestinal resection is afforded by the experiments of Evans and Brenizer, who resected 33, 37, 41 and 50 per cent of the combined jejunum and ileum with recovery, and the discovery of a more localized hypertrophy, particularly marked in the neighborhood of the anastomosis. The resections were followed by another series in which 76.1, 84.6, 86.5, 87.3 and 92.0 per cent of the total mesenterial intestine was removed. The first two animals of the series recovered, while the last three died of inanition, after living thirty, fifty-one and ninety-seven days respectively. The last animal of the series was very fat, which probably enabled him to live off his own tissues for the greater length of time. In the last animals, no hypertrophy was noted, these being cases where the resection had exceeded the limit where a compensation could be established. Certain of our own animals showed a similar behavior, which is not unlike the human cases that made an operative recovery, and died later of inanition. These authors conclude that an animal can practically always survive the removal of from one-third to one-half of the combined jejunum and ileum, but that resections greater than this may exceed the limit for which a compensation can be made.

In the autopsies upon our own animals, nothing was found of an abnormal nature outside of the intestine itself. Dogs Nos. 1, 2 and 10 were fairly well nourished, while No. 9 was thin. The macroscopic changes in the intestines in Nos. 1, 2 and 10 were all practically alike. Careful measurements from the landmarks left at the time of operation showed that there had been no increase in the length of the intestine. Within the small limits of error that one might reasonably allow, the dimensions were the same. If any real lengthening had occurred, it was so slight that it could not be distinguished from a possible error in measurement. The intestines showed a marked increase in the transverse dimensions, which to the naked eye appeared to be about twice the size of the gut at the time of operation. This increase was confirmed as the intestine was taken from the body and compared with the piece that was removed at the operation. In all cases except No. 9, in which the writer did not see the autopsy or control the preservation of the specimens, the hypertrophy varied between 30 and 100 per cent. It involved both the stomach and the cæcal end, although the relative difference in the size between these two portions of the intestine was preserved.

There is, however, apparently a limit beyond which a hypertrophic response can be obtained, where simply an intestinal incompetency is established and the dogs die of slow starvation, prolonged and modified by the amount of food they can assimilate through the abbreviated gut. In such cases, the compensatory hypertrophy is absent. In other cases, the response may be partial, but the dog may never gain its full weight, and hence be only a partial recovery. Dog No. 12 is an example of this type. The hypertrophy was not nearly so marked as in the Dog No. 2, and the partial compensation is indicated in the functional inefficiency of the intestine as shown by Professor Underhill's metabolic determination in contradistinction to those obtained by Erlanger and Hewlett on Dog No. 2, under conditions of an average diet.

It was difficult to ascribe a cause to the transverse hypertrophy, and the failure of the intestine to enlarge markedly in its longitudinal dimension. The only plausible interpretation appeared to lie in the mesentery. The mesentery, while providing for the normal elasticity of the gut, naturally holds the intestine somewhat fixed in its longitudinal dimension. This might be looked upon as the factor involved, although in such an elastic organ a slight lengthening of the gut may have been present and escaped observation, owing to the contraction of the longitudinal layer of the tunica muscularis. If this were the case, however, the increase could not have been in excess of 15-30 cm., the usual probable error in careful measurement.

In Dog No. 12, where the small intestine was short-circuited, the differences between the two segments are beautifully shown (Fig. 1). The functional segment is seen markedly hypertrophied while the short-circuited portion appears about one-half its size. The transverse folds, due to the contraction of the longitudinal muscle, are seen in both sections of the gut. In all other animals, no evidences of compensation or change were observed in the stomach or large intestine; both remained macroscopically normal. In this case, however, there is a marked dilatation of the stomach, with an almost complete atrophy of the omentum, but the large intestine appears normal. Sections of the stomach in these animals show that the parietal cells are considerably more prominent than the chief cells, the histological picture resembling not a little that given by Heidenhain for starving animals. No other changes were observed in the stomach. Microscopic study of the colon in Dog No. 12 showed it to be of normal structure and thickness, making it evident that the colon had undergone no morphological changes to compensate for the functional removal of the small intestine.

It might be suggested that the difference in size between the two segments of ileum in Dog No. 12 was partially due to an atrophy of the functionless portion of the gut, especially as Cunningham has described such changes after short-circuiting for physiological experiments. Plant, who kept a dog alive two and a quarter years with a short-circuited loop which he had used for the study of fat absorption, found absolutely no evidences of atrophy. The sections of the short-circuited ileum of Dog No. 12 were the most perfect I have seen, and showed absolutely no evidences of degeneration of any sort. Furthermore, the comparison of the size of the gut with that of normal dogs revealed no changes other than in the

remarkable clearness of the histological picture. This, I believe, to be due to the absence of fats undergoing absorption which tend, when the intestine is thrown into the fixing fluids, to cause a separation of the epithelium from the stroma of the villus.

Monari states that there is a regeneration of the villi, that is to say, that they are more numerous after the operation than before. This appears to be a random statement, for only by the most accurate methods of observation could one say definitely that there was an increase in the number of villi. At the outset, I may say that I expected to find a regeneration of the villi, for, according to the manner of their development, it seemed like a simple method of providing for an increase in the epithelial surface of the intestine. In order to prove or disprove a regenerative process, I counted the villi and estimated the area of the intestine removed at operation and autopsy. The number of villi in a square millimeter were counted a great many times in each 10 cm. of intestine and the average taken. From this, the number in each 10 cm. of intestine were computed. Like the length of the intestine, the total number of villi varied in different animals. In the series of animals from which I computed the number of the villi, including not only our operated dogs, but several normal ones as well, the total varied between 800,000 and 1,200,000. The number does not vary to any great extent between the upper and lower portions of the intestine, although the cæcal is much smaller than the stomach end of the gut. This indicates that the villi are smaller in this region, a fact which can be proved by a comparison of villi from the two sources in the same animal, or demonstrated by sections of the healed suture in these extreme resections, where the upper end of the intestine is anastomosed to the lower. Here, where the two types are found on either side of the scar, on the duodenal side of the cicatrix they are about 50 per cent larger than on the cæcal side, if there has been an extensive resection of the gut.

In comparing the portions of intestine removed at operation with those obtained at autopsy, approximately the same number of villi were found in each 10 cm. of intestine. In the same unit of area, however, only half as many were counted in the hypertrophied intestine as in the piece removed at operation. Inasmuch as there had been an increase in the total area of each 10 cm. of nearly 100 per cent, the villi had naturally not increased in number, but had simply increased in size. In this way, it was possible to exclude positively at least any extensive regeneration of these structures which Monari believed took place. Although, as was shown later, the hypertrophic process involved the submucosa and muscularis as well as the mucosa, this was not apparent from a macroscopic inspection of the intestine. It gave the appearance, however, that the operation had yielded an intestine that was magnified about one diameter. This hypertrophy was more apparent in the upper than in the lower end of the gut.

To determine the exact effect of the resections upon the intestine itself some accurate method must be employed. The comparison of sections by the eye must be supplemented by a mathematical registration of the differences in the intestine before and after the operation in three dimensions. Monari simply used a control dog and, in this way, could not exclude the possibility of individual variation between his control and his operated animals. Accordingly, to obtain the desired comparison, and still to avoid all possible errors by the use of control animals, I reconstructed a portion of the intestine removed at the operation from the region of the upper suture in Dog No. 10. After the animal had lived a year and a half, another piece was reconstructed from the region just above the line of anastomosis, where the upper and lower ends of severed intestine had been united. In this way pieces were obtained that were not separated from each other during life by more than 5 cm. Observation shows that there are no differences in the structure of the intestine under these circumstances, although the intestine is smaller at the cæcal than at the stomach end, and that the several coats are not so large or well developed in the distal portion of the gut. Any differences, therefore, between these two reconstructions must have been caused by the operation, and the model made from the resected pieces would represent the normal conditions for that region of the intestine. Such a model shows a number of facts interesting in themselves as well as being of importance for comparison, for it represents the normal anatomy of this portion of the intestine; but it should be remembered that the description applies only to the dog's intestine. A glance at Fig. 2 reveals the following interesting facts. The normal villus can scarcely be looked upon as having a definite shape, as it is a more or less plastic element, influenced in its form by factors in its environment and in its architecture. The profile picture of a villus seen in sections, for example, gives no real conception of its form, as one must reconstruct many of them in three dimensions to appreciate the extreme variability of their contours in a fixed condition, and to discover the factors that determine its shape under these conditions. Under perfectly relaxed conditions of the tunica muscularis, as well as the muscle bundles within the intestine itself, the form of the villus would probably be columnar with rounded ends. As soon as the musculature of the intestine contracts, or when the intestine is thrown into the fixing fluid, the villus alters this form. This alteration, due to the contraction of the muscular wall of the intestine and the intrinsic musculature of the villus, does not represent an abnormal condition, but records permanently conditions that occur regularly in the intestine. The form of the villi has been variously described as cylindrical, fusiform, club-shaped, etc., but a glance at Fig. 3 shows that there are no constant shapes, as the form is largely an adaptation to external pressure and all of these types may be found in the same region. This pressure is exercised under normal conditions by a contraction of the muscular coats, which may, naturally, act in one direction or the other by the single action of either the outer or inner layer of the tunic separately, or in both directions at once by the simultaneous contraction of both sheets of muscle together. In such a specimen, the villi always fit into each other, leaving only a small space between their epithelial surfaces. Club-

shaped, cylindrical, fusiform villi, and those with pointed ends occur side by side, closely packed together, taking on a form to fit the space they have to occupy. At times they are triangular in cross sections and may be folded or grooved to fit adjacent villi that impinge upon them. When one finds a villus with pointed ends, ordinarily there are club-shaped elements next to it. In general, the end toward the submucosa is smaller than the end toward the lumen of the intestine, a relationship, however, due to the contraction of the combined muscular coats. When the longitudinal muscle bundles within the villus contract, the epithelium on the surface of the villus is thrown into a series of transverse folds (Fig. 3). This illustrates excellently the pump action of the villus, which is a notable factor in aiding the movement of the intestinal lymph. By the contraction of the musculature in its stroma, the central lymph space of the villus is emptied into the submucosal plexus, where its return is prevented by the valves situated at that point. Villi in a state of contraction are shown by the folding of the surface epithelium.

In many cases, the ends of the villi are rounded, while in others they are pointed and irregular. Likewise the sharp contraction of the intrinsic musculature of the villus as it is thrown into fixing fluids, often draws the stroma away from the epithelium and allows the latter to hang loose, like the finger of a partially withdrawn glove. By some investigators this has been considered a normal relationship, but it is obviously an artifact, as the stroma draws the membrana propria away with it and allows the epithelium to hang free and loose. Such free tips of epithelium are nicely shown in the model represented in Fig. 2. It may be well to observe, however, that such pictures are much more readily obtained during digestion, for the accumulation of the fat globules beneath the epithelium during absorption seems to facilitate the ease with which the stroma may be retracted from the epithelium. Instances where the stroma projects into the epithelial tips, however, are not abnormal. The average size of the villi in the same region of the intestine is constant, although their power of contractility gives them, under fixed conditions, a slightly different caliber. Unfortunately, owing to the scale selected for the model, it was hardly possible to show the relationship of the crypts to the villi. They are represented by the solid portion of the model under the villi.

After the resection of large portions of the intestine, say from 50 per cent to 70 per cent of the entire small intestine, or from 60 per cent to 83 per cent of the combined ileum and jejunum, very marked changes take place in the structure of the remaining portion of the intestine. These modifications are shown in the model represented in Fig. 3, which was made from a portion of the intestine of the same dog as Fig. 2, and was not situated more than three or four centimeters from it before the resection of the intestine took place. Thus all of the differences shown by this preparation are the direct results of the operation. At the first glance, the enormous hypertrophy, which reaches about 100 per cent, is seen. Not only the villi are enlarged, but also the portion of the mucosa forming the crypts shows an increase in size approximately equal to that of the villi. So far as the form of the villi are concerned, the relationships are practically the same. In the increase of the epithelial surface by the hypertrophic process, there seem to be a few more club-shaped villi, which may indicate a slightly greater increase in the mucosal as against the muscular coats of the gut, or may be due to a greater degree of contraction of the latter. In the hypertrophied specimen, great irregularity is observed in the form of the villi, but, as in the normal intestine, this represents an adaptation on the part of the villus to the space which its neighbors allow it to occupy. There is, naturally, the same interaction of the individual villi upon each other's form. Numerous longitudinal folds occur in the villi near the base to allow them to fit in with the adjacent elements, and, where the longitudinal bundles of muscle in the villus are contracted, the epithelial surface is thrown into a series of transverse folds, giving it a corrugated appearance. In the hypertrophied specimen, this condition illustrates the pump-like action of the villi even better than the contracted elements in the normal intestine.

The microscopical changes that take place in the intestine after the resections, may be seen in the two figures drawn from sections of the gut before and after the operation. Fig. 4 is taken from the upper end of the resected portion of the intestine removed at the first operation, while Fig. 5 is from the portion of the ileum just above the first suture; that is to say, the tissue from which the sections were cut, like that from which the reconstructions were made, was situated in the same segment of the gut before the operation was undertaken.

The hypertrophic process induced by the resections involves all the layers of the intestine, but it is more patent in the tunica mucosa than in either the submucosa or muscularis. In the mucosa, the hypertrophy occurs in the region of the crypts as well as in the villi. The latter show an increase in the amount of their stroma, although it maintains the same characteristics as the stroma of the normal villus. The reticulum framework is a little denser and its nuclei are more numerous, otherwise the connective tissue is unchanged. The longitudinal bundles of smooth muscle are proportionately enlarged, and the vessels appear more tortuous. On comparing the epithelium of the hypertrophied villus with the control specimen, it is observed to be distinctly higher than normal, the hypertrophy reaching, perhaps, 30 to 50 per cent in excess of the cell's original size. The nucleus also takes part in this process with a slight increase in size, but otherwise, the cell retains all of its usual characters, such as the granular protoplasm and the cuticulated border toward the lumen of the intestine. Goblet cells are numerous about the base and sides of the villus as in the control specimen, but there is no increase relatively in the number of these cells, such as Monari described, although with enlarged epithelial surface there is a numerical excess over the control specimen. No mitotic figures are seen in the epithelium covering the villus.

It is not possible to make out great changes in the stroma of the region of the crypts, but like the epithelium of the villus, these elements themselves are both hypertrophic and hyperplastic. The chief increase is in the length of the crypts,

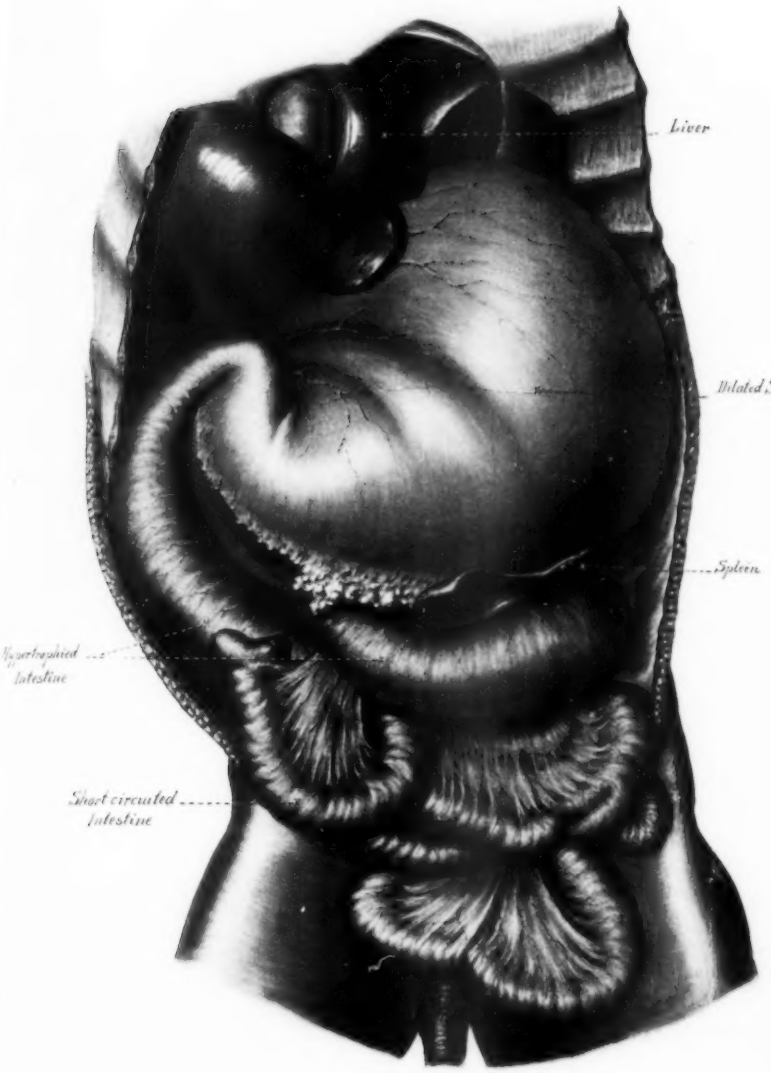

FIG. 1.

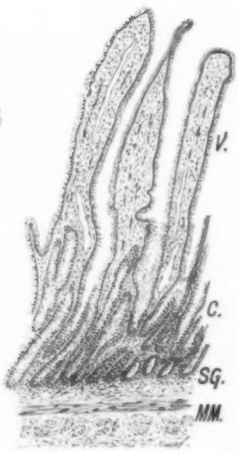

FIG. 4.—Section of the intestine removed from Dog No. 2, taken from the stomach end of the resected portion in the first operation.

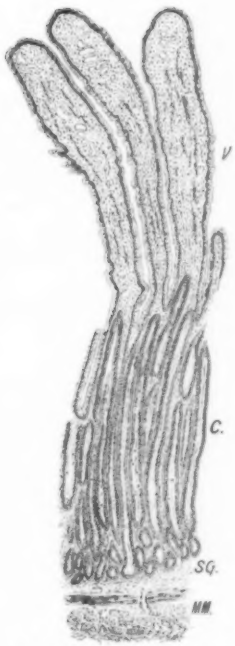

FIG. 5.—Section of the mucosa taken from the duodenal side of the upper suture in Dog No. 2; that is to say, from the same region of the intact intestine as the section shown in Fig. 4.

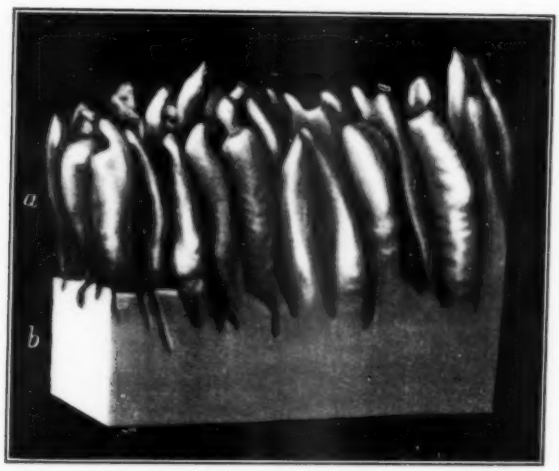

FIG. 2.—Reconstruction of a portion of the duodenal end of the intestine removed at operation from Dog No. 10.

FIG. 3.—Reconstruction of a portion of the intestine from the same animal as Fig. 2. Taken from a region just above the healed intestinal suture. Before the operation, the pieces of tissue from which Figures 2 and 3 were taken were separated from each other by not more than a few centimeters. Reconstruction on the same scale as Fig. 2.

and in the presence of occasional cystic dilatations at their extremities. These ampullæ-like widenings rarely exceed four or five times the diameter of the crypts, and ordinarily show little evidence of pressure or pressure atrophy, although in one or two instances I have observed points where epithelium was flattened to a third of its normal height. These cysts are filled with a coagulated granular mass and desquamated degenerating cells. The proportion of goblet cells has not increased. In the lower half of the crypts there are numerous karyokinetic figures, probably representing the regular regeneration of the epithelium of the villi and the crypts, according to the observations of Bizzozero and Heidenhain.

In Dog No. 1, however, the karyokinetic figures are much more numerous than in the other three cases. This may, of course, represent only a very active regeneration, but it seems quite possible that it is associated partly with the hypertrophic process, for, in this case, I have also found occasional mitotic figures in the stroma of the villus. This dog was killed before the total compensatory increase in the epithelial surface was established, and thus the excess of karyokinetic figures over those that are present in Dogs Nos. 2 and 10, can be explained. It is extremely difficult to form an opinion concerning the changes in the stratum fibrosum and the stratum granulosum, for they vary to a marked extent with the degree of distension of the gut, but it is probable that, in common with the submucosa, these layers are somewhat enlarged.

The muscle tunics have distinctly hypertrophied, but of the two, the inner circular layer is larger when compared with the control specimen. This is in accord with Monari's observations. The Peyer's patches have also taken part in the general enlargement, and in Dog No. 1 evidences of cell division are occasionally found. The enlargement of these structures are by no means proportional to the hypertrophy of the mucosa, however, in my specimens, but owing to the impossibility of distending both portions under exactly the same pressure, this point is of no moment, as the comparison cannot be made absolute.

After the consideration of the morphological and metabolic changes resulting from a shortening of the small intestine, it is now possible to consider these modifications of structure and function in their relations to each other.

In trying to determine the cause of the hypertrophic process that occurs after the extirpation of a large portion of the gut, there are a number of factors to be taken into consideration. In the first place, there is no question that more mechanical work is done by the portion that is left. The simple mechanical effect, however, of the increased amount of food and water taken, as evidenced by the ravenous appetite and great thirst displayed by the animals after the operation, seems inadequate to explain the change, for these, like the normal appetites, are more probably simply symptoms of a tissue thirst and a tissue hunger induced by the reduction of the normal absorption of food stuffs. If the term "work" is used in the sense of an increased functional activity, then, to be really explanatory of the hypertrophic process, it must be analyzed into its several factors.

As was shown by the investigations of Diliberti-Herbin, the immediate metabolic effect of the operation is to diminish, to a marked degree, the absorption of fats and nitrogenous substances. According to Vitali's observations there is, in all probability, also an initial decrease in the absorption of carbohydrates, whereas after the compensation is fully established by the hypertrophic process, these food stuffs are completely utilized. This diminished absorption or increased excretion with its consequent destruction of the normal balance between ingestion and elimination, makes it essential, if the nutrition of the animal is to be maintained, either for the remaining portion of the intestinal mucosa to improve in the efficiency of its power of absorption, or else to proliferate and increase its area as a compensation for the lost portion of the gut.

As we have seen, the second process takes place and we may say then, that the diminished absorption of fats, nitrogenous substances, and carbohydrates causes a proliferation of the intestinal mucosa, and at the same time of the other coats of the intestine. As time passes, there is a gradual decrease in the excretion of these substances (Diliberti-Herbin) and with it goes hand in hand an increase in the absorbing surface of the intestine, as is shown by the findings in Dogs Nos. 1, 2 and 10. The metabolic disturbances may, under favorable conditions of diet and life, finally disappear, and the nutrition become practically normal (Erlanger and Hewlett, Dogs Nos. 2 and 10). When this condition is attained, we find that the mucosa in a dog with 70 per cent of the small intestine removed (Dog No. 10) has hypertrophied to the degree shown in Fig. 3.

This ratio between area of absorption and the degree of elimination proves positively that there is a relation between the area of the intestine and the nutrition of the animal. We may even go as far as to say that, under normal circumstances and average conditions of diet, there must be a minimal relation between the area of the intestine and the size of the organism.

The intestine, like other organs, probably rarely functions up to the limit of its capacity. Like the heart and other organs, there is a reserve power rarely called into use. This excess in the intestine may, perhaps, be measured by the resection of small portions, where the metabolic reaction is nil, or is buried in the normal variations. But when the limit of this reserve is reached, the diminished absorption involves the adaptative powers of the remainder of the intestine and a compensation for the loss is established in a hypertrophy of the remainder. In this case, the parallel between the hypertrophy of the heart and the hypertrophy of the intestine is perfect, although the functions and factors involved may be entirely different. Moreover, the comparison may be carried still further, for the adaptation, as in the heart, although admirably calculated to compensate for the loss, lacks the efficiency of the normal organ. Like a machine run to its full capacity, it is liable to break down. This was admirably shown in the case of Dogs Nos. 2, 9 and 10, where under favorable condition of diet and life, the hypertrophy secured

a functional adjustment like that of a normal dog. As soon as these favorable conditions ceased to obtain, the insufficiency of the adaptation became evident, and nitrogen and fat were eliminated in a much higher percentage than in a normal animal. If adjustment is too fine, as in Dog No. 9, the break leads to death, like a broken compensation of the heart, or to some such condition as the prolapsus recti, induced in Dog No. 10 by the profuse diarrhœa.

The history of the operations on the human intestine parallels in all respects the experiments upon our animals. Schlatter's case particularly, with the diminished absorption which persisted for almost two years, reached finally such a stage of compensation that his patient, an Italian, could eat the frugal diet of his people. In this case there is little question that the hypertrophic process was slowly taking place.

A last and most interesting point in connection with the functional adjustment produced by this hypertrophy lies in the relationship of the epithelial or absorbing surface of the intestine before and after adaptation has taken place. In Dog No. 10, from which the reconstructions were made, the hypertropy of both villi and crypts led to an increase of almost twice their original size. In this case 238 cm. of the intestine was resected, and the portion remaining, as shown at autopsy, was 96 cm., making a total length of 334 cm. In such more or less cylindrical structures, as the villi and crypts, an increase of 100 per cent in their size would lead to an increase of 400 per cent in surface. That is to say, the surface of the enlarged villus or crypt would be four times that of the original element.

Bearing this fact in mind, I have endeavored to compute the degree to which the compensatory hypertrophy restores the original epithelial surface of the intestine. A computation of this character, naturally, cannot be made more than generally accurate, but the figures indicate that the compensatory enlargement of the crypts and villi, when the process is complete, approximately restores the original surface of the intestine. That a hypertrophic mucosa, even should it have the area of a normal intestine, is not as efficient an agent for the absorption of the essential part of the digestive processes which are carried on in the intestine, is shown by the ease with which it becomes incompetent to do its work—a fact to which attention has been called above, in Dogs Nos. 2, 9 and 12.

It was noted in discussing the autopsy findings that the stomach and colon play no demonstrable part in the compensatory process. Barring conditions in Dog No. 12, where the stomach was markedly dilated, no changes of note occurred in these organs. Thus, there is a pretty definite basis for the view that the different portions of the alimentary tract exercise a fairly specific function, and while, as has been shown, an animal or a man may live without either stomach or colon, a certain amount of small intestine is necessary for the maintenance of life. Indeed, after the efforts at regeneration which the organism makes to restore lost parts of the intestine, it is probable that there is a definite ratio between the size of the organism and the epithelial surface of the intestine under ordinary conditions of diet and life.

This is made even more probable by the interesting experiments of Babák, who tested the question on frogs. Frog larvæ may be brought up either as herbivora or carnivora. Babák divided a large series of larvæ, feeding one group with a vegetable and another with a meat diet. The groups raised as herbivora invariably had larger intestines than those fed on meat. This indicates the influence of the diet on the size of the intestine, but might equally well be used to express the demands which the organism makes for a certain absorption surface, which may be demonstrated either by reducing that which it possesses or changing the nature of its diet to one less easily assimilated. Pauchet states in his paper that he intended to bring about a lengthening of the intestine of his patient by feeding a vegetarian diet. If, however, this idea were carried out without judgment, it might be made equivalent to a more complete resection of the intestine.

So far as the practical bearing of the researches upon animals with shortened intestines are concerned, the results do not justify us in establishing a limit of resection which may be definitely applied to the human intestine. Even the series of cases of extensive resection of the human ileum set no definite boundary which it is fatal to exceed, as the maximum measured instance in the literature, a case of 540 cm., was not only immediately successful, but caused astonishingly little metabolic disturbance, although the ultimate outcome was death from inanition two and one-half years later. From the experimental standpoint, this limit will not be established until the method of fractional resection is thoroughly applied, as the interesting work of von Haberer on the kidney shows. At present, even the results of primary resection are colored too much by such factors as the age and condition of the animal or patient, the length of the intestine and the functional efficiency of the mucosa. As a matter of fact, notwithstanding the effort of numerous investigators to establish this limit, its interest is only academic, and its application will only be of use in affording us, perhaps, indications as to diet and a probable prognosis of the case. These facts are shown by an inspection of the table of cases given above, when more than 200 cm. of the intestine was resected. In these instances, the procedure was never an operation of choice, as the extent of the resection was established by the pathological process and not by the surgeon. The surgical rule has been and will continue to be, the removal of the minimum amount of the gut permitted by the morbid condition, and the prognosis will depend chiefly upon the factors given above; namely, age, condition, resistance, nutritive efficiency, and the length of the unresected segment of the gut. To these factors might be added, as Fantino has pointed out, the ability of the remaining part of the intestine to inaugurate compensatory processes. There are, apparently, instances when portions of the intestines are functionally incapacitated some time before the necessity of an operation, a condition which would bring the case to the operating table with a partially compensated or hypertrophied intestine, and thus facilitate the subsequent compensation for the resected segment of the gut. Such a state of affairs would almost be equivalent to a fractional re-

section, where the hypertrophic process would be partially established before the limit of resection is reached.

Generalizations from our animal experiments might lead us to assume that 50 per cent of the human intestine might be removed, perhaps with severe nutritive disturbances, but with no probability of death. A study of the cases, however, shows the possibility of death from inanition where only 300 cm. have been resected. Mayndl's case, which died of marasmus after the removal of 284 cm., was possibly complicated by the cachexia caused by the carcinoma cæci which necessitated the resection. If we are justified in generalizing from these cases, we may say that there is not great danger in removing as much as 275 cm. of the small intestine, but that beyond that limit death from marasmus may occur. As a result of the operation, there is the possibility of severe nutritive disturbances after the resection of so small an amount as 198 cm., as is evidenced by the case of Schlatter. On the other hand, the resection of much larger amounts may yield relatively little post-operative interference with the metabolism, as is shown by Brenner's patient, from whom he removed 540 cm., but in the end, lead to inanition and death.

The metabolic experiments indicate that the diet in these cases should be rich and easily assimilated, but it should not contain too great a percentage of fats. The complete utilization of the carbohydrates of the diet suggests the advisability of increasing these elements of the food, especially in some easily assimilated and usable form, like the simple sugars.

CONCLUSION.

1. As much as 50 per cent of the total small intestine in dogs may be removed without fatal results. The animals may gradually return to a condition of practically normal weight and metabolism when maintained on the favorable diet under good conditions. Resections of 75 per cent and even more of the total small intestine may be survived, but such animals are not liable to show a true recovery, *i. e.*, a return to normal weight with the establishment of a good compensatory process.

2. At first, the animals suffer from a severe diarrhœa, ravenous thirst and appetite, and loss of weight, from which they gradually recover until conditions may return to those of a normal animal. They remain, however, extremely sensitive to unfavorable conditions of diet and living.

3. Metabolic studies on such animals show that there is a marked increase in the excretion of the nitrogenous, fatty, and carbohydrate elements of the food. The elimination may reach 66 per cent of the diet content. After compensation is established, on a rich, easily assimilated diet, digestion goes on as in a normal dog, except for an increase in the amount of intestinal putrefaction, as indicated by the amount of indican in the urine. An increase in the amount of fats in the food may lead to an increased elimination of nitrogen and fats to a point about 25 per cent above normal. The carbohydrates, on the contrary, are absorbed to a degree considerably above normal after the compensation is established.

4. The compensatory process consists in a hypertrophy as well as hyperplasia of the remaining portion of the small intestine. There is no regeneration of either the villi or crypts. Computation makes it probable that in favorable cases approximately the original epithelial area of the intestine is restored by the hypertrophic process.

5. As in animals, about 50 per cent of the small intestine may be resected without much danger of serious consequences in the majority of cases. The resection of smaller amounts may, however, be followed by severe metabolic disturbances, and even inanition and death. Human cases behave in general like the animals. They show similar metabolic disturbances. In one case there was distinct evidence of a compensatory process. No regeneration or hypertrophy has ever been reported in a human case. There are over fifty-eight cases reported in the literature where over 200 cm. of the small intestine have been resected. The mortality is 16 per cent, which is probably much lower than it should be, owing to the greater probability of successful cases finding their way into the literature.

6. The metabolic disturbances in human cases bear no definite relationship to the amount of small intestine resected. Five resections of over 400 cm. have recovered, while death from inanition has resulted from the resection of 284,289,300 and 350 cm., respectively. Profound digestive disturbances have resulted from the removal of 192 and 204 cm. of ileum. In human cases, factors like difficulties in measurement, the pathological condition, the total length of the intestine, and the resistance of the patient undoubtedly modify the result, and explain the apparent discrepancies between the amount of intestine resected and the subsequent metabolic disturbances.

7. The prognosis in human cases should be guarded. Apparently successful resections may, for lack of suitable compensation, succumb ultimately to a slow process of inanition.

8. The experiments and the series of human cases emphasize the specific function of the three segments of the gastro-intestinal tract. Neither the stomach nor colon is able to compensate for the loss of large portions of the small intestine.

9. Resection of the human intestine is almost never an operation of choice. The surgical rule has been, and will continue to be, a resection of the minimum amount allowed by the pathological conditions. From the metabolic studies, it would seem wise to give these patients a rich and easily assimilated diet, poor in fats and relatively rich in carbohydrates.

REFERENCES.

1. Albu: Berl. klin. Wchnschr., 1901, XXXVIII, 1248.
2. Axhausen: Mitth. a. d. Grenzgeb. d. Med. u. Chir., 1909, XXI, 55.
3. Babák: Arch. f. Entwicklungsmechn. d. Organ., 1906, XXI, 611.
4. Cannon: Am. J. M. Sc., 1906, n. s., CXXXI, 563.
5. Cunningham: J. Physiol., Lond., 1898, XXIII, 209.
6. De Filippi: Arch. ital. de biol., 1894, XXI, 441.
7. Denk: Wien. klin. Wchnschr., 1907, XX, 1649. Mitth. a. d. Grenzgeb. d. Med. u. Chir., 1909, XX, 215. Idem, 1911, XXII, 146.
8. Diliberti-Herbin: Gazz. med. ital., 1903, liv, 401.
9. Erlanger & Hewlett: Am. J. Phys., 1901-02, VI, 1.

10. Evans & Brenizer: Johns Hopkins Hosp. Bull., 1907, XVIII, 477.
11. Flint: Arch. f. klin. Chir., 1906, LXXX, 988.
12. Lane: The Operative Treatment of Chronic Constipation, London, 1909.
13. Mayo: Trans. Am. Surg. Ass. 1909, XXVII, 310.
14. Monari: Beitr. z. klin. Chir., 1896, XVI, 479.
15. Plant: Am. J. Phys., 1909, XXIII, 65.
16. Riva-Rocci: Gazz. med. di Torino, 1896, XLVII, 121.
17. Schlatter: Cor.-Bl. f. schweiz. Aerzte, 1899, XXIX, 417.
18. Senn: Experimentelle Beiträge zur Darmchirurgie, Basle, 1892.
19. Spassokukozkaja: Russk. Vrach., 1906, V, 35.
20. Storp: Deutsche Ztschr. f. Chir., 1907, LXXXVII, 313.
21. Trzebicky: Arch. f. klin. Chir., 1894, XLVIII, 54.
22. Vitali: Ref. Centralbl. f. d. Grenzgeb. d. Med. u. Chir., 1903, VI, 440.
23. Underhill: An. J. Phys., 1911, XXVII, 366.

THE BEHAVIOR OF THE BLOOD PLATELETS IN TOXEMIAS AND HÆMORRHAGIC DISEASE: A PRELIMINARY REPORT.*

By W. W. Duke, M. D., Kansas City, Missouri.

I desire to report in brief a review of thirty-one cases of hæmorrhagic disease studied with especial reference to the relationship between hæmorrhage and the platelet count; also clinical and experimental results which are thought to throw light on some of the factors causing pathologic fluctuation in the platelet count. In studying hæmorrhagic disease a means, described by the writer in a paper published elsewhere, called the bleeding time was used. The bleeding time denotes the duration in minutes of a hæmorrhage proceeding from a small cut in the lobe of the ear. It must not be confused with coagulation time—a term which denotes the rate at which blood clots.

Of the thirty-one cases studied, seventeen had normal or slightly increased platelet counts, fourteen had exceedingly low counts, below 65,000. (The normal count ranges from 200,000 to 400,000.) The group having the low counts differed clinically in many respects from the group having normal or increased counts—in fact the outspoken cases of the low platelet group presented a symptom complex simulated in its entirety by none of the cases having higher counts.

Discussion in this paper is confined to the low platelet group of cases. The severer of these were purpura hæmorrhagica, *i. e.*, purpura with hæmorrhage from one or more mucous membranes. The milder cases presented sometimes little or no purpura and little or no hæmorrhage from *normal* mucous membranes. Frequently the only evidence of hæmorrhagic diathesis was excessive hæmorrhage from some local condition; for example, bleeding from intestinal ulcers, bleeding varices in cirrhosis of the liver, profuse menstruation. One symptom constant in the severer cases and frequently present in the milder ones was a tendency to bleed from every abrasion of the skin. Some patients would bleed for hours from a mere scratch. In consequence of this tendency the bleeding time was greatly prolonged (twenty minutes to two hours). The prolonged bleeding time is thought to be the most characteristic symptom of the disease.

The platelet counts were enormously reduced in every case showing a bleeding time of ten minutes or more. In the milder cases it was below 65,000; in the severer cases below 10,000 and frequently below 1000.

A decrease in the platelet count has been considered characteristic of purpura hæmorrhagica by Denys, Hayem, Bensaude and others. My results show that the low counts are not confined to purpura hæmorrhagica, but are found also in cases of hæmorrhage due in part to local causes. I have also seen two cases of purpura hæmorrhagica in which the platelet count was normal. One of the cases was purpura hæmorrhagica associated with urticaria and intestinal crises (Henoch's purpura); the other was purpura hæmorrhagica in cholæmia. These cases had normal bleeding times and differed therefore in this respect from the cases with the low platelet counts.

Direct transfusion of blood was carried out in three cases. This procedure was followed by an immediate and complete relief of the hæmorrhagic diathesis lasting about three days. The bleeding time in one case was reduced from ninety minutes to three minutes, and in another from thirty minutes to three minutes. On the fourth day after transfusion hæmorrhage began again, and the bleeding times were again prolonged. The only striking change in the blood, to explain this period of relief, was the rise in the platelet count—evidently the direct result of transfusion. In two cases, where observations were made, the counts were 6,000 and 20,000 before transfusion, and 129,000 and 89,000 respectively directly after transfusion. The platelet counts decreased steadily after the first day, and on about the fourth day reached their previous low levels. Simultaneously with this decrease in number of the platelets the hæmorrhagic diathesis returned. There was no change in the coagulation time of the blood during the period in which the patients were observed. The period of relief was thought to be due directly to the presence of the blood platelets.

In one case of severe purpura hæmorrhagica, counts were made almost daily for a period of about four weeks. During this period the bleeding time was enormously prolonged whenever the count was below one thousand, and was shortened sometimes to ten minutes, when the count rose to about ten thousand. Where the count is at such a low level as this a slight rise seems to cause a noticeable amelioration of symptoms.

Where observations were made it was noted that the hæmorrhagic diathesis appeared simultaneously with the disappearance of the platelets, persisted as long as the platelet

*Read before the Johns Hopkins Hospital Medical Society, February 19, 1912.

count remained extremely low and disappeared as soon as the platelet count rose. Occasionally the purpura cleared up or the hæmorrhage was less severe or stopped completely for a time during a period in which the platelet count was still low. A determination of the bleeding time, however, demonstrated that the improvement was apparent but not real, and that the patients were still bleeders.

Routine platelet counts were made on patients with diphtheria, nephritis, and phthisis. In this series the hæmorrhagic diathesis of the type described appeared in three cases. These were the only cases in which the platelet count was enormously reduced.

In a series of 41 experiments on animals, an effort was made to produce purpura hæmorrhagica experimentally by treating rabbits and dogs with benzol, tuberculin, and diphtheria toxin. These agents were chosen on account of the frequency of purpura hæmorrhagica in benzol poisoning, tuberculosis, and diphtheria. Severe purpura hæmorrhagica was produced in only one experiment. This was by the use of a sublethal dose of diphtheria toxin. In this animal, two weeks after the administration of the toxin, the platelet count, which had previously risen and reached a height of 1,700,000, suddenly fell so low that platelets could hardly be found in the counting chamber. On the day on which the platelets disappeared from the circulation petechiæ appeared on the ear, and the bleeding time, obtained from cutting the skin, was enormously prolonged. On the following day the animal's cage was spattered with blood. This condition, since there was a petechial rash, and a tendency to bleed from every abrasion, corresponded with the disease as seen in man. The hæmorrhagic period persisted three days and disappeared on the fourth. It was on this day that the platelet count rose. Neither purpura nor prolongation of the bleeding time was noticed in two other rabbits treated with the same dose of toxin, nor in six rabbits treated with a larger dose. In these animals the platelet count did not descend below the critical level.

Purpura hæmorrhagica conforming to the type described, has been observed by me complicating chronic ulcerative colitis, spastic constipation, tuberculosis, diphtheria and aplastic anæmia. Cases evidently of this type have been reported by Hayem and Bensaude in lymphocytic leukæmia, hæmorrhagic smallpox and tuberculosis, by Pratt in nephritis and by Selling in aplastic anæmia due to benzol poisoning.

The condition has been observed then complicating a variety of diseases and has been produced experimentally. The one feature in common was the reduced number of platelets. That there exists therefore a causal relationship between an absence of blood platelets and a certain form of hæmorrhagic diathesis seems highly probable. The disease includes most but not all cases of purpura hæmorrhagica, and in addition many cases of local bleeding.

In studying blood coagulation in this series it was found, as noted by Denys and Hayem in their cases, that the coagulation time was not delayed, in fact it was often even shorter than normal; also that fibrin was formed in abundance and had a normal microscopic appearance. It was seen further that in animals with severe benzol poisoning and a markedly reduced platelet count, the fibrinogen content of the blood was normal. As discovered by Hayem blood free from platelets, although it clots rapidly, does not retract from the sides of a vessel containing it and extrude serum. Whether this phenomenon is to be attributed to abnormal fibrin or whether it is due to the fact that platelets are not present to anchor together the filaments of fibrin, is not clear. Absence of retractility was found in this series of cases whenever there was a marked reduction in the platelet count.

In accounting for hæmorrhagic diathesis it is difficult to eliminate entirely certain possibilities which have been frequently suggested as a cause of purpura in this and other types of disease, namely: abnormal vessel walls, abnormal coagulation, capillary emboli, etc. It may be that such conditions play a contributory rôle in the pathogeny of this disease. The tendency to bleed, however, can be accounted for without assuming their presence, as follows: hæmorhage is not checked to any great extent by a clot such as is seen on the surface of a wound, but chiefly by an intravascular thrombus—a structure having an entirely different architecture and mode of formation. A clot formed from still blood consists of a homogeneous mixture of platelets, red cells, leucocytes, fibrin etc. A thrombus formed from flowing blood, on the other hand, as demonstrated by Hayem and others, has a totally different structure and is made up to a large extent of masses of agglutinated platelets. It has been repeatedly demonstrated that after injury to a vessel wall, platelets are the first element to adhere to the injured intima, and are deposited in enormous numbers before fibrin is laid down in demonstrable quantity. From the structure of the thrombus alone, it would be natural to expect that an absence of platelets would cause an abnormality in its formation or initiation, and would therefore be a cause of prolonged bleeding whether the fibrin-forming factors were normal or not. The fact that an individual may bleed for two hours from a pin prick, when platelets are absent, is sufficient evidence that thrombi do not form in this condition, and suggests therefore that the rôle played by platelets is an essential one.

The studies on hæmorrhagic disease brought to light facts thought to show a possible cause of pathologic variation in the platelet count. In the experimental work it was observed that the subcutaneous injection of large doses of diphtheria toxin (doses which proved fatal in three to four days) causes an immediate fall in the platelet count. Sublethal doses, on the other hand, cause an enormous rise followed by a fall, or simply a rise in the count. The same general rule applies to animals treated with benzol. The injection of large doses of benzol causes a rise in the count followed by a rapid fall, while the use of smaller doses causes a marked rise. The injection of tuberculin causes only a rise in the count, even when enormous doses are used. These experiments seem to show that a clinical pathologic variation in the platelet count is in many diseases the effect of a toxin on the platelet-forming elements (possibly also on the platelets in the blood stream). In large doses the toxin acts as a poison and in small doses as an irritant, or first as an irritant and then as a poison. Where the platelet irritant is a strong one (diphtheria toxin for example) the count is

almost as frequently increased as decreased. Where the irritant is mild (as in tuberculosis for example) the platelet count is usually increased, but in case of an unusually large dose or of a peculiarly susceptible individual it may be reduced. This hypothesis fits well with my counts in diphtheria and phthisis. In diphtheria I found the change observed by Hayem in many acute diseases, and called by him a "hæmatoblastic crisis," to be the rule; that is, the count was usually reduced (in one case to 3,000) during the febrile period of the disease, and increased during convalescence (highest count 750,000). The opposite change, however, was also observed; that is an increase in the count during the febrile period and a fall during convalescence. In advanced phthisis my figures show that the count was usually increased, sometimes enormously so (highest count 1,100,000). In two cases, however, it was enormously decreased for a short time, once below 1,000.

SUMMARY.

To summarize, then, variation in the platelet count in many diseases is largely the effect of toxins, some of which in small doses increase the count and in large doses decrease it. When the count descends below a level of about sixty thousand there may be an abnormal tendency to bleed. When it descends below about ten thousand, this tendency is always present, and when below one thousand, is present in its most severe form.

In conclusion I wish to express my thanks to Dr. Hugh Cabot and Professors Murphy, Romberg and von Noorden for the privileges granted me in their clinics; to Dr. J. H. Wright for suggestions about methods for counting platelets; to Dr. G. H. Whipple for his kind assistance in making fibrinogen analyses and Dr. L. Selling for suggestions as to the use of benzol.

AN ALVEOLAR TUMOR OF THE CAROTID GLAND WITH SARCOMATOUS TRANSFORMATION.

By PAUL G. WOOLLEY, M. D., and FRANK FEE, M. D.

(From the Laboratories of the Cincinnati Hospital.)

INTRODUCTION.

By FRANK FEE, M. D.

Of recent years tumors of the carotid glands have been receiving more and more attention from surgeons, and cases appearing from time to time in surgical literature show that they are less rare than formerly supposed. These glands derive surgical importance from the fact that they are so closely related to the carotid arteries, the deep jugular vein and such important nerves as the sympathetic, hypoglossal, lingual and vagus. This intimate connection to the carotids necessitates ligation of these vessels in about 60 per cent of the cases. Then, too, any or all of the above-named nerves may be injured or completely severed during operation.

Tumors of this gland are not easily diagnosed, as shown by the early reports. They have been mistaken for enlarged lymphatic glands, lipomata and even goitre. In my own case, I had made a diagnosis of carcinoma of the lymph glands, following what I took to be a carcinoma of the thyroid gland. It was my intention, first, to remove this lymph gland, which caused the patient the greater discomfiture, and then should her condition warrant to remove the thyroid. The removal of this required one and one-half hours and I discontinued the operation after its removel. In this case I feel that I was extremely fortunate in not having to ligate the vessels or injure the nerves.

Keen admirably describes the diagnostic symptoms and signs as follows:

The diagnosis based on positive and negative facts. The Positive Facts: 1. There is a tumor arising in the region of the bifurcation of the carotid; that is to say, about on a level with the upper border of the sternocleidomastoid, but when it has reached any size it is only partly covered by this muscle. 2. The tumor is moderately movable horizontally, but not vertically. 3. It is usually ovoidal in shape. 4. As a rule it is smooth and not lobulated. 5. It is a singular tumor and not made up of a coalescence of several tumors, as in tuberculous glands. 6. There may be bruit and thrill, but this is rare and not marked. 7. There is transmitted but non-expansile pulsation. 8. It may cause bulging of the wall of the pharynx. 9. The pupil is occasionally contracted. 10. It will usually grow slowly at first, and possibly, shortly before the surgeon sees it, more or less rapidly. 11. It will have existed for a number of years. 12. The consistence is neither very hard, nor very soft, but elastic. The Negative Facts: 1. There is no pain. 2. As a rule it is not tender. 3. There is no disturbance, as a rule, of the pneumogastric, either as to its cardiac or laryngeal functions. 4. There is no disturbance of the sympathetic nerve. 5. There is no change in the pupil, except occasionally. 6. So far as the patient is concerned, there are usually no subjective symptoms, but the aid of the surgeon is sought on account of a slowly or rapidly growing deformity, and if the tumor is growing rapidly there may be also fear of its results.

My patient, Mrs. X., aged 68, was fairly well developed, but poorly nourished. She first noticed a goitre developing five years ago. She had consulted several physicians at various times, and had taken thyroid extract for periods of one month on several occasions. The tumor on the right side of the neck, independent of the goitre, made its appearance about two years ago, and had gradually grown larger.

Examination.—Pulse 110, respiration 20, temperature 99.6°F. Heart, lungs and kidneys negative. The pupils reacted to light and accommodation and were normal in size. The neck was considerably emaciated. The thyroid gland was

found to be enlarged on both sides, but more marked on the left where it was adherent to the trachea but not to the skin. The larynx was pushed well to the left side causing paroxysms of difficult breathing. Between the sternocleidomastoid muscle and the right lobe of the thyroid a mass about 2½ inches long and 1½ inches in diameter was found. Its shape was distinctly ovoid and its smooth capsule could be easily felt through the skin. With the patient lying on her back a distinct bruit could be heard, but upon turning face downward this disappeared. Pulsation could be easily felt, but was not expansile in character. Its consistency could be likened to that of an enlarged non-suppurating lymph gland. Its mobility was limited to horizontal movements, lateral motion being arrested by a small attachment to the thyroid gland.

Operation.—June 9, 1910. An incision was made over the most prominent portion of the tumor and its capsule exposed. With blunt dissection the internal and external carotid arteries were exposed and separated from the tumor. Ligation of these arteries was not necessary. Owing to the tedious character of the operation and the poor condition of the patient it was thought advisable not to attempt to remove the thyroid gland. Drainage was inserted in the lower angle of the wound which was closed with silk-worm gut.

Remarks.—The patient rallied from the operation and did fairly well for several days. A slight purulent discharge developed in the wound and later symptoms of a mild septicemia appeared following which the patient gradually grew worse until July 13, or 23 days after the operation, when she died.

A post-mortem examination was not made. The tumor was sent to Dr. Woolley for pathological diagnosis.

PATHOLOGIC REPORT.

By PAUL G. WOOLLEY.

Tumors of the carotid glands are not common. The reasons for this are probably two, though we know but one, and this is that the glands themselves are of inconstant occurrence. For example, Funke found carotid glands in but one of eight fœtuses, and Gomez found them in but five of fifty human bodies. In four of these only one gland was present. This inconstancy has been remarked by all observers from the time of Haller to the present.

The site of the carotid glands (*glomera carotica*) is the region of the bifurcation of the common carotid artery. In this region they are found, as a rule, situated posterior and mesial to the bifurcation so that they come to lie nearer to the internal carotid. They are supplied by a single nutrient artery from the arterial trunk nearest to which they lie, and they are connected to this trunk by a fibrous pedicle, called the ligament of Mayer, which is continuous with the capsule of the gland and the adventitia of the artery. In it the nutritional vessel runs, and passes into the gland, accompanied by numerous medullated and non-medullated nerve fibers, at the hilus. The capsule of the carotid bodies send numerous septa into the organ and divide it into the so-called "secondary nodules," each of which is divided into smaller cell masses commonly called the *Zellballen*, which are composed of the cells which are characteristic of the organ. These cells are large, rounded or polyhedral, have a clear protoplasm, and contain large, round, well-stained nuclei. They lie closely adjacent to the endothelial layer of the capillaries. This appearance is, as Mönckeberg says, best seen in the glands of young individuals, since with increasing age the fibrous tissue increases and separates the cells from the blood vessels. Marchand believed that these typical cells are derived from vascular loops. Paltauf also believed them of vascular origin, but rather from perithelium. Schraper could find no evidence of endothelial origin. Stilling observed chromaffin cells in the carotid bodies and hence came to the opinion that the glands are similar in origin to the adrenals. Kohn also, mainly upon the basis of the presence of chromaffin cells, sympathetic ganglion cells and the abundance of non-medullated fibers, thought that the *Zellballen* were composed of cells derived from sympathetic cells. But up to the present time there is no defined consensus of opinion as to the origin of these glands.

It is therefore impossible to refer to tumors arising in the carotid glands except in morphologic terms and to speak of them as Kaufmann does as "alveolar tumors," for until there is greater certainty regarding their origin it seems wiser not to use the term angiosarcoma, perithelioma, carcinoma, or endothelioma. According to Stieda, Rabl, du Meuron, Maurer, and others, the carotid glands are derived from the third or fourth branchial cleft. Katschenko, Paltauf and Szymonowicz, Marchand and Mönckeberg believed that they originate from the perithelium of the carotid arteries. Luschka and Kohn think them of sympathetic nervous system origin like the medulla of the adrenal.

The tumor, which serves as the basis of this report, measured 6.5 x 3 x 3 cm., and weighed 35 gm. It had the general shape and appearance of a small clean potato. It had been preserved in formalin. The surface was generally smooth and was modified by the appearance of flattened or rounded elevations which projected but slightly above the general surface of the tumor mass. At one point there was a teat-like projection that measured 2.5 x 1 cm. The general color was bluish-gray modified irregularly with yellowish patches, or mottled with brownish-red. The teat-like projection, which, like the main tumor, was lobulated, had a generally light yellowish-white color with smaller brownish mottlings. The whole mass of the tumor was enclosed by a smooth thin capsule from which five strands passed into the tissue between the lobules. Except for the resistance caused by these penetrating strands, the capsule could be readily removed. It was not adherent to the substance of the tumor except at a few places. At no place was there evidence of a direct penetration of the capsule by the tumor, though there were a few small dark lappets that seemed to perforate the thicker parts of the capsule, but these lappets also were covered by a very delicate membrane. Such projecting masses measured not more than 3 mm. in length. In consistence the tumor was for the most part firm, but at one pole it had a partially spongy or cystic feel. It was rather friable, and after removal of the capsule, especially from the

large teat-like process, could be separated partially into its lobules.

The color of the cut surface varied. At one pole (the upper) it was generally yellow, but with small grayish areas that were minutely cystic in appearance, and with other bluish hyaline zones surrounding the yellowish, more solidly cellular, areas. Practically one-third of the entire tumor had this structure. The central third was rather more generally mottled with yellowish-brownish-red and bluish hyalin, the latter apparently due to the presence of the homogeneous contents of small cystic spaces. The yellowish parts had a granular friable appearance. The lower third of the tumor mass was predominantly cystic, the individual spaces of which ranged from the size of a pin point to 3 mm. in diameter. In color this part was dark, reddish-brown or brown, and with more hyalin than the other parts of the tumor. Between the cysts the tissue was, as a rule, grayish and occasionally of a whitish homogeneous appearance like hyaline fibrous tissue. The teat-like mass was pale or yellowish and almost uniformly solid. It contained one large cyst with brownish-red hyaline contents, near the outer third, and a second small one, with almost black contents just at the base.

Bits of the tumor were taken from various parts, imbedded in celloidin and paraffin, cut, and stained with hematoxylin and eosin, iron hematoxylin, orcein-thionin, van Giesen and Mallory's aniline blue. The sections stained by the latter method were taken from tissue that had been treated with picric acid followed by ammonium bichromate.

Histologic Structure.

In a general way sections showed that the tumor was alveolar and cystic—as a matter of fact the predominating feature of the tissue was its exquisite alveolar arrangement.*

The larger cystic spaces were lined with a columnar or cuboidal epithelium that was regularly arranged and which occasionally showed a tendency to intracystic papillomatous overgrowth (Fig. 4). These lining cells showed an almost complete uniformity of structure; the nuclei were vesicular and were provided with deeply staining nucleoli, and surrounded by a reticulated protoplasm in which no extraneous substances were visible. An occasional cell showed enormous increase in size, which, with the rounded contour and accentuation of the reticulation and vacuolation, seemed to indicate an edematous degenerative condition. The contents of these cysts were composed of a hyaline, usually slightly acidophilic, clear, homogeneous, or partially granular material, in which were imbedded larger or smaller numbers of red blood corpuscles, polymorphonuclear and mononuclear leucocytes, and pigmented epithelioid cells. Certain of such cystic spaces were filled with blood. In others blood had very probably been present, but had been absorbed so completely that but little pigment remained, though the pericystic connective tissue, in the meshes of which pigment-carrying cells could be seen, were deeply stained. There was no sudden transition between these cystic structures and the following which approached in their appearance the follicles of the thyroid. These follicular structures were of two main sorts: one in which the most exquisite interacinous growth was discovered (Fig. 1), and one in which there was no such picture. In both the lining cells were cuboidal, sometimes flattened and as a rule one row in thickness. The contents of such structures had a hyaline or colloid appearance and this was, as a rule, clear and achromatic, or, occasionally, somewhat basophilic, staining blue with thionin, and hematoxylin. This material seemed to be, in at least some instances, the product of cell degeneration, for frequently one could see in it the faint shadows of cell outlines. In other instances no structure could be observed. In other areas this follicular structure was less in evidence because of the papillomatous overgrowth which was as characteristic and delicate as the interacinous growths of certain adenomas of the breast, and this was so accentuated at times that comparatively large areas were seen which were composed of rambling, interlacing columns of cells that produced secondary acini by their interweaving (Fig. 6). In some of these complexes the cells were of the typical high columnar type with the nuclei distal to the centers of the cells. The areas that were less cystic and less follicular and more glandular in character were characterized by appearances that were but accentuations of those described above. The general difference was that there was an increase in epithelial cells with no evident tendency to cyst formation or to intracystic or intra-acinous papillomatous overgrowth (Fig. 2). In such places the cells were arranged, sometimes in rounded or compressed masses with some or no evidence of a central space, sometimes in parallel columns several cells in thickness.

In none of the areas thus far described was evidence of malignancy encountered. The cell masses and columns were sharply limited by the supporting tissue and mitotic figures were found only in exceptional instances. As a matter of fact there was no evidence that growth has been anything other than slow. But there were certain parts of the tumor in which the line of demarkation between parenchyma of supporting tissue was indistinct and in which there was evidence of invasion—of infiltration (Fig. 3). In such areas there was less of an orderly arrangement of the cells. Cell columns were irregular and were composed of many layers of irregularly arranged cells in which mitotic figures were more frequent than in other parts of the tumor. In the region of the tumor where this atypical, more or less solid structure was found, there was also some cystic and even intracystic growth (Fig. 3). The walls of such cysts and the papillary growths were composed of several layers of cells—often many—but in these layers there was a lack of order. Moreover the cells varied enormously in size and shape. There were no columnar cells and few cuboidal. All or nearly all were polymorphous with large nuclei and with relatively less granular or spongy protoplasm. Again, whereas the parenchymatous cells were arranged in masses, as a rule, there were areas where they were scattered in the con-

* For the purposes of description, the tissue will be divided according to its gross microscopic structure, it being understood that all transitions occur between different general types of arrangement, and that this division is purely artificial.

FIG. 1.

FIG. 3.

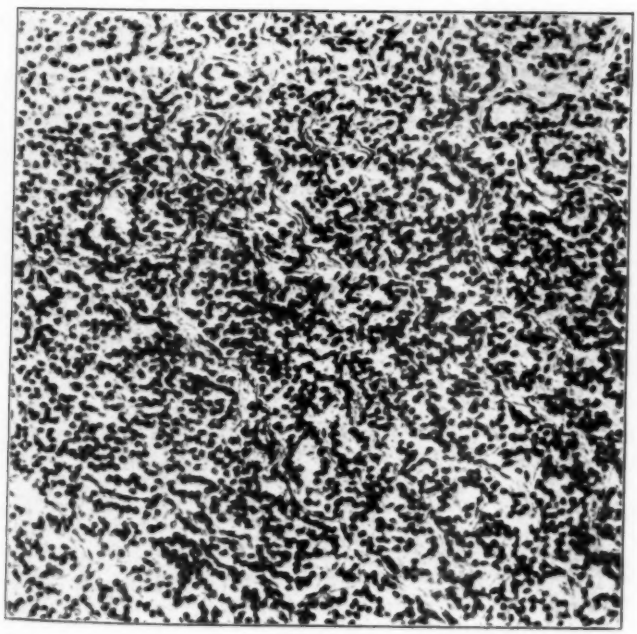

FIG. 2.

FIG. 4.

nective tissue, sometimes in irregular slender columns, but also in small groups, and even singly. There was the further interesting fact, also, that, in the region in which there was evidence of infiltration from the side of the parenchyma, there were also symptoms of increasing activity on the part of the connective tissue (Fig. 3). It was not merely hyperplastic, but unusually cellular, rich in ovoid and spindle-shaped nuclei and contained many mitotic figures. The fibers were more or less arranged in bundles, some of which were cut in cross, some in longitudinal section. There was a fairly abundant infiltration with small round cells.

Elsewhere the connective tissue was in only moderate amount; it had a generally healthy appearance, but also showed occasional hyaline areas.

The larger blood vessels showed but little change. In the purely follicular parts they were either normal in appearance or showed a moderate amount of hyalinization. In the malignant parts they showed a more widespread hyaline change.

It is difficult to estimate the relationship, if one exists between the small blood vessels and the tumor. There were areas in which there was a perivascular arrangement of cells, but this was never typical. There was no palisade formation, and the cells had none of the usual clear transparent appearance of the typical perithelium. The same was true of the malignant parts of the tumor, so that one is inclined to think that growth proceeded along the vessel sheaths, rather than that it originated in them. In these ambiguous locations there was always an apparently normal endothelial lining in the vessels. There was also no evidence at any place of an intercellular reticulum (Fig. 7), a fact that speaks neither for nor against endothelioma, since, as I have shown, a reticulum may or may not be present in such tumors, though the tendency is to the former condition. Yet there is evidence, though not of the best, that at least a part of the tumor may be of endothelial origin. In some suggestive places there were all transitions from hyperplastic endothelial cells through solid cellular masses of epitheliod cells to areas in which the central parts of such masses had undergone degeneration producing pseudocystic figures (Fig. 3), in which the central contents are evidently cellular detritus and in which cell shadows can still be seen. In some of these also there was evidence of deposition of lime salts from a bare lacking to deeply staining granulation.

Résumé of Microscopic Appearance.

I. The tumor showed an exquisite alveolar structure, with all transitions from large cystic structures, containing vestiges of hemorrhages, to solid cellular masses and strands.

II. In the larger cystic spaces the lining cells were columnar or cuboidal and of but one layer (as a rule) in thickness. There was typical intracystic proliferation.

III. In the more solidly cellular parts the cell masses often showed central degeneration giving rise to the appearance observed in cylindromas. In some places there was evidence of deposition of lime salts in the degenerated material.

IV. There was evidence of perivascular progression; some of perithelial proliferation and some of endothelial overgrowth.

V. The tumor, in general, had the characters of a benign growth, but there were areas in which there was distinct evidence of malignant change, both in the stroma and parenchyma.

The Cells of the Tumor.

In the foregoing description mention has been made of the fact that the more or less cystic spaces were lined with epithelium that showed all transitions between a high columnar and low cuboidal form, and that these cells, as a rule, were arranged in single rows. Occasional pigmented cells of two types were encountered—those that were phagocytic carrier cells, and those which were apparently not carrier cells. There were other cells that presented enormous variation in size, form, and microscopic appearance, both as regarded the general appearance and the nuclear structure. Such variations were present not only in the epithelial portion, but also in the stroma.

Certain changes have also been observed in the appearances of the vascular endothelial cells, and in the cells immediately associated with the blood vessels. It is with these appearances that the following paragraphs will be concerned:

According to various authors there are at least three types of parenchymatous cells in the carotid bodies. The predominant type is large, more or less irregular in form, but with the tendency to be cuboidal or polygonal. These cells have vesicular nuclei with distinct chromatin granules and a centrally placed nucleolus. Another type is one which has more or less of a lymphoid appearance. The protoplasm is relatively scant; the nucleus is round, deeply staining and contains chromatin granules. The third type of cell is the so-called chromaffin cell of Stilling.

Concerning the origin of these latter cells there seems to be no doubt. They are epithelial, derivatives, like those of the adrenal medulla, of sympathetic nerve cells.

On the other hand the origin of the predominating cells of the carotid bodies is in dispute. It is believed by some investigators that they are very closely associated with vascular endothelium—that they are in effect outgrowths of such a tissue. Others suppose that though they are derived from endothelium they have become independent to the same extent as the adrenal cortical cells. Upon either supposition tumors would be classified with the mesotheliomata, but in the first instance they would represent vascular tumors, *i. e.*, true endotheliomata; in the second they would be classified with the tumors, which, like those of the adrenal, have no evident vascular origin or arrangement. There seems to be no consensus of opinion on these taxonomic questions, though it is generally believed that the glands are of endothelial origin. If it can be shown that there is a definite relation between the alveolar portions of such tumors and the sarcomatous portions, then we shall have some evidence to support the view of the endothelial relationship of the cells. Such support will be derived in this way: True endotheliomas do not show a typical alveolar appearance such as is presented in carotid tumors, though it is true that they may show sarcomatoid variations. Tumors of

the adrenals, to use a single instance, may originally have an alveolar structure and appearance and may also, in the original growths, as well as in their metastases, show a structure that corresponds exactly with that shown by typical sarcomata. Examples of this have been published by Jores, Woolley and Meakins. If then it can be shown that there is a true transition from adenomatous (carcinomatoid) structure to sarcomatoid, we shall be in possession of evidence of mesothelial origin of the carotid gland.

The cells of the tumor under consideration are generally of the large cell type. They are polymorphous. The nuclei are large, oval, round or occasionally angular. They are more or less vesicular with a reticulated structure, the fibrils of which radiate from a distinct central chromatin granule or nucleolus to the peripheral chromatin-studded limiting membrane. The depth of staining reaction varies considerably, but the structure is generally the same in all the cells. Most of the nuclei show, beside a nucleolus, smaller chromatin granules. The protoplasm is, as a rule, relatively abundant and frequently achromatic, though usually and but moderately acidophilic. It is reticular in structure, and occasionally contains granules or droplets of a light or brownish-yellow material that resembles the lipoid granulations of other organs (Fig. 5). The form of these cells vary as already has been mentioned from high columnar, through low cuboidal, to polymorphous. The more columnar cells are relatively richer in protoplasm, and the nuclei tend to be oval. The angular nuclei are probably due to fixation. The size of these cells varies enormously, ranging from some as small as mononuclear leucocytes to others ten times as large. In such huge cells the nucleus and protoplasm are both increased, the gain in the latter being greater. The same general structure is preserved. No more cells of lymphoid type have been encountered than one could account for on the basis of an hematogenous origin.

It therefore appears that the alveolar portions of the tumors are composed of but one type of cell, that of which the primitive *Zellballen* are composed in the normal gland. The pigmented cells perhaps need explanation. The pigmentation appearances of some of these is evidently due to the remains of blood pigment. In others, such as are situated at considerable distance from areas of hemorrhages, this explanation is not so satisfactory. The suggestion occurs that these cells are related in a more or less direct fashion to the cortical cells of the adrenals. They do not show the characteristic color and appearance of chromaffin cells.

Concerning the relation of the cells of the alveolar portions of the tumor to the blood vessels there is little to be said. They were evidently, so far as our observations are concerned, entirely unrelated, directly at least, to the endothelium of the vessels. Even at points where there was the wheel or concentric arrangement, there was no evidence of endothelial origin, but rather of perithelial progression. Though the tumor was rich in small blood vessels and capillary networks there was no place at which a relation between tumors and endothelium seemed possible.

In many alveoli, especially in the malignant portions of the tumor, there was a gross morphologic appearance that suggested endothelioma. Here the alveoli were often lined with one or many rows of flattened cells about a central hyaline or bluish laked or granular mass which was due to central alveolar degeneration. The appearance produced was that encountered in cylindromas. Such central masses were evidently composed of degenerated cells, for shadows of cells and nuclei could be seen with the proper powers of the microscope. Around such alveoli the capillaries appeared healthy. It was in such localities that the greatest variation in the size of the cells was observed. Syncytial formations also occurred.

At points where infiltration was in evidence, there was less variation in the size of the cells. At such places the columns or single rows of cells and isolated epithelial cells were of generally uniform appearance. They were rather more spindle-shaped than the alveolar cells, but evidently not of the sarcoma type. The stroma in which they were imbedded had, however, undergone malignant change and was composed of spindle cells of a rather slender variety. It was infiltrated with small round cells and a considerable number of polymorphonuclear leucocytes.

In résumé we may say: (1) The cells of the alveolar parts of the tumor and of the stroma were apparently autonomous, though both exhibit malignant changes, and neither had any apparent close or definite relation to the endothelium of the blood vessels.

(2) That the cells of the alveolar portion were of one main type and corresponded in general appearance with the large cells of the original *Zellballen*. The proliferated and infiltrating stroma cells were of the spindle cell variety.

(3) The changes in the blood vessels seemed to be relatively unimportant. There were very occasional places where there seemed to be some localized hyperplasia with a tendency to the production of polypi composed of cell masses with no evidence of cell boundaries (syncytium). This process seemed to have no particular connection or relation with the other changes in the tumor.

We believe that but two other tumors of this sort (*i. e.*, showing definite sarcomatous change) have been reported; that of Leithoff, and that of Kaufmann and Ruppaner.

BIBLIOGRAPHY.

Many references mentioned in the text have been consulted, but there seems to be no need to extend the bibliography by merely repeating references given in other works. Therefore, only what seem to be the most complete and modern articles are cited here.

Kaufmann and Ruppaner: Deutsche Ztschr. f. Chir., 1905, LXXX, 259. (Contains a complete review of the literature.)

Mönckeberg: Ziegler's Beiträge, 1905, XXXVIII, 1.

Gomez: Am. J. M. Sc., 1908, CXXXVI, 98.

Keen and Funke: J. Am. M. Ass., 1906, XLVII, 469 and 566.

The questions relating to the structure and development of mesotheliomas are discussed in a complete and comprehensive way by Adami in his Principles of Pathology, 1910, Vol. 1. In this volume the work of Jores, Woolley, Meakins and others is cited and the references given (pp. 677 and 706).

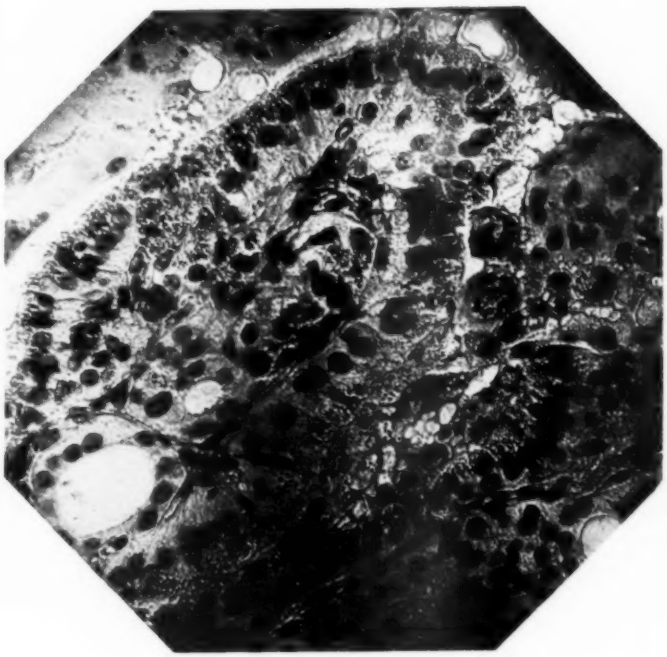

FIG. 5.

FIG. 6.

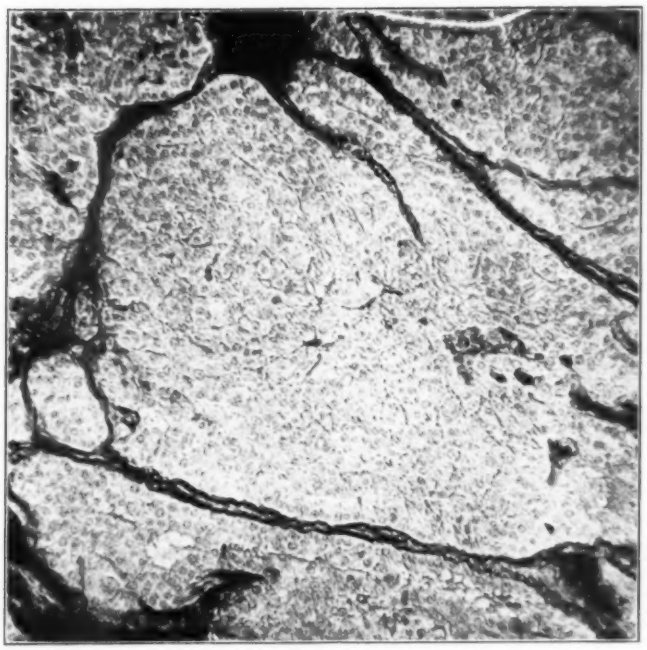

FIG. 7.

ILLUSTRATIONS.

(Photomicrographs by Dr. Charles Goosmann.)

FIG. 1. Section of the tumor showing the delicate intracystic papillomatous structure of certain parts.

FIG. 2. Section showing the almost solidly adenomatous structure of certain parts.

FIG. 3. Section showing pseudocystic spaces, and evidences of malignancy in parenchyma and stroma.

FIG. 4. Section showing canalicular, cystic and intracystic growth.

FIG. 5. Section showing the structure of certain parts of the tumor in which the cells contain a lipoid-like (?) pigment.

FIG. 6. Section showing an accentuation of the appearance shown in Fig. 4.

FIG. 7. Section of the more solid portion of the tumor showing the arrangement of the reticulum.

NOTES ON NEW BOOKS.

Emergency Medical and Surgical Aid. A Manual of First Aid for Laymen, with Special Reference to Industrial Accidents. By ERNEST A. WELLS, M. D. (*Hartford, Conn.: Published by Ætna Life Insurance Company.*)

Any person who will make himself master of the directions given by Dr. Wells in this well arranged handbook will, when the emergency arises, be able to give useful assistance. There are however in the author's directions several points to which exception may be taken. Under "Drowning" he states that there is no possibility of resuscitation if the patient has been completely submerged for seven or eight minutes. As it can hardly ever be known how long the patient has been completely submerged, efforts at resuscitation should be prolonged for as much as an hour or more.

Again under "Freezing" the writer says: "Gradually thaw out the frozen parts with warm water and rubbing. The tradition that you must use snow or ice water is absurd." The tradition may be absurd from one point of view, but is sensible, as there is little doubt that if warm water is used, it will be used too hot, and the frozen parts will be burned, as the patient has no feeling in the affected portion and so is unable to measure the heat of the water.

Under "Fits" Dr. Wells says the patient "may bite his tongue, it will do no harm and you cannot help it. Do not try to pry his mouth open, for you may break his teeth, and there is no sense in it." This advice does not recommend itself to the reviewer, who feels that efforts should be made to prevent the patient severely biting his tongue, of course without using so much strength as to break the teeth.

The outfit for a first aid is more suited to a doctor's office than to a layman's, but in large industrial institutions it would be wise to fit up a room with this stock.

It is a pity that the title page and the title on the cover do not correspond, and in a second edition the text will require some revision to perfect the English.

Serum Diagnosis of Syphilis and the Butyric Acid Test for Syphilis. By HIDEYO NOGUCHI, M. D., etc. Illustrated. Second Edition. $2.50. (*Philadelphia: J. B. Lippincott Company, 1911.*)

The second edition of Noguchi's well known work upon serum diagnosis shows important revisions and additions to the first edition and will be welcomed by all those interested in serological methods and their application to clinical medicine.

One of the most valuable additions to the present volume is the chapter on the effect of treatment upon the serum reaction, which also discusses in some detail the results after treatment with "606." This chapter is one of great interest and importance to both the laboratory worker and the practising physician.

The essential facts of hemolysis and complement fixation are explained with simplicity and clearness. Too much stress, perhaps, is laid upon the author's modification of Wassermann's original reaction, and parts of the book give the impression that it was written as much for the purpose of advancing the author's views, as for presenting the general subject of serum diagnosis. This tendency is apt to give the beginner an undue preference for the author's own modification. To those familiar with both sides of the question, however, this presentation of the author's views is of great interest and quite stimulating, even if not wholly accepted.

The glossary at the end of the book is of great aid to those who are not familiar with the terms used in serum work. The statement, however, that complement fixation is synonymous with complement deviation, a term introduced by Neisser, is inaccurate or at least requires further explanation.

The bibliography is unusually complete and of great aid to the reader who wishes to consult original sources and go deeper into the subject. The book is well written, full of valuable data and statistics and can be heartily recommended to all those interested in the subject of serum diagnosis. R. H. M.

International Clinics. Edited by HENRY W. CATTELL, M. D., and collaborators. Vol. I. Twenty-second Series. $2.00. (*Philadelphia and London: J. B. Lippincott Company, 1912.*)

The paper of most interest in this volume is Flexner's on "Experimental Poliomyelitis," but others by Walsh on "The Masks of Diabetes" (much better than its title might indicate), Taylor's "Venereal Diseases in the United States Navy," and articles by Hill, Parke Weber, Kopetzky and Brooks will find many readers. We select a few names simply to indicate the varied nature of the papers rather than any special preference, for the internist, the surgeon, and general practitioner will each find something to hold his attention.

The Surgical Clinics of John B. Murphy, M. D., at Mercy Hospital, Chicago. Vol. I. Number I. Octavo of 133 pages, illustrated. Published Bi-Monthly. Price per year: Paper, $8.00. (*Philadelphia and London: W. B. Saunders Company, 1912.*)

These "Clinics" have been recorded by a stenographer at the time the patients were operated upon by Dr. Murphy, and his talks are presented verbatim. This is a new venture both on the part of the author and the publishers, and one that cannot be commended for general adoption. Such informal talks may give one a good picture of the lecturer, and at times be entertaining and instructive reading, but they lack system, and the very method of their presentation is not attractive in book form. A lecturer must often repeat himself in an informal talk to doctors or students, but in his permanent writings he should show more style and finish. It is difficult to believe that these "Clinics" can prove of any real service to the profession, except as a record of Dr. Murphy's agreeable personality and his ability as a surgical teacher. Many will value them as we all like to preserve the spoken words of our friends, but they are two diverse and disjointed to serve for thorough teaching, which, after all, must be the real end to be aimed at in a series of clinics.

Kursus der Normalen Histologie. Ein Leitfaden für den praktischen Unterricht in der Histologie und Microscopischen Anatomie. Von RUDOLF KRAUSE, A. O. Professor der Anatomie an der Universität, Berlin. Illustrirt. Mk. 22.50. (*Berlin und Wien: Urban & Schwarzenberg; New York: Rebman Company, 1911.*)

This very attractive manual is evidently intended as a guide for those who give courses in histology as well as for the student. The author has a short talk with the instructor in the introduction, in which he protests against the prevalent neglect of technical procedures in histological courses, allowing the student to depend upon his courses in pathological anatomy or even clinical medicine for a working knowledge of this subject.

The first hundred pages are devoted to a fairly thorough description of the various technical methods used in the study of histology. The remainder of the book, some 430 pages, contains 208 beautiful colored illustrations made from original drawings by the author. The text consists almost entirely of explanations or demonstrations of the figures which are numbered and carefully labelled. Each paragraph is headed by its appropriate title, the magnification of the specimen and the technique employed in its preparation with references to the first part of the book where the methods are described. The illustrations are excellent, and well chosen, the descriptions clear and concise.

This book will doubtless be a great boon to that great class of students who wish detailed and thorough demonstrations. Students of a different sort will find it convenient in verifying or correcting their own independent observations. It will be useful to all as a reference handbook of up-to-date technique.

Honan's Handbook to Medical Europe. A Ready Reference Book to the Universities, Hospitals, Clinics, Laboratories and General Medical Work of the Principal Cities of Europe. By JAMES HENRY HONAN, M. D., etc. With Maps of Berlin, Edinburgh, London and Paris. $1.50. (*Philadelphia: P. Blakiston's Son & Co., 1912.*)

This handbook is exactly what it is stated to be in the title, and Dr. Honan has compiled in excellent form a large amount of most useful information for students and doctors who intend going abroad for study or simply to visit some of the foreign clinics. This manual will prove itself invaluable to such travellers for the author gives data about 17 university cities in Germany, 6 in Switzerland, 6 in Great Britain, and others in France, Austria, Sweden, Denmark, Norway, Roumania, Greece, Belgium, Italy, Russia, Spain and Holland. With this book as a guide, medical travelers will find their way about much more easily in these centers, and Dr. Honan will, we are sure, have both the sincere silent and expressed thanks of many of his confreres for his work.

Second Review of Some of the Recent Advances in Tropical Medicine, Hygiene and Tropical Veterinary Science. Being a Supplement to the Fourth Report of the Wellcome Tropical Research Laboratories at the Garden Memorial College, Khartoum. By ALFRED BALFOUR, M. D., Director, and CAPTAIN R. G. ARCHIBALD, M. B., in collaboration with CAPTAIN W. B. FRY, M. R. C. S., and CAPTAIN W. R. O'FARRELL, L. R. C. P. $3.75. (*Published for Department of Education, Sudan Government, Khartoum. London: Baillière, Tindall & Cox, 1911.*)

All students of tropical diseases should be most grateful to the authors of this work. Here they can quickly find references to all the latest and best articles on practically every variety of disease occurring in the tropics. The reviews are well prepared and the number of articles that have been read and digested is enormous. While no such book can be complete yet it is likely that very few papers of importance have been overlooked, and it is to be hoped that the Wellcome Laboratories will continue to publish these Reviews. Medical literature grows apace and it is absolutely requisite for the student to have such books to assist him, as without them he would be quite lost in the mass of papers to be looked up on any tropical disease. In view of the size and handsome appearance of the book its price is cheap.

Minor Surgery. By LEONARD A. BIDWELL, F. R. C. S. Illustrated. (*London: University of London Press, 1911.*)

The author aims to give simple directions for the management of everyday minor surgical work, and in addition he has added very brief descriptions of certain major operations. Important points are emphasized by being printed in heavier type.

The book is similar to a number of others already on the market and offers very little, if any, additional information.

J. S. D.

Manual of Physiology for Students and Practitioners. By H. WILLOUGHBY LYLE, M. D., etc. Illustrated. $4.00. (*London: Henry Frowde, and Hodder & Stoughton, 1911.*)

A compressed text with few illustrations by an Examiner in Physiology appearing in its first edition. So far as it attempts to present the subject the book is open to little criticism. But the author's self-defined limits necessarily makes the book didactic, and therefore, lacking in inspiration to the student. Those interested in the science of physiology and the further introduction of this science into all medical work cannot but regret such a publication, however much it may supply the demands of students preparing for licensing examinations, since knowledge gained therefrom will scarcely stimulate effort towards the solution of problems either in the laboratory or clinic.

Progressive Medicine. Edited by HOBART AMORY HARE, M. D., Assisted by LEIGHTON F. APPLEMAN, M. D. Vol. I, March 1912. (*Philadelphia and New York: Lea & Febiger, 1912.*)

The reviews of current literature in this volume cover the Surgery of the Head, Neck, and Thorax, Infectious Diseases Including Acute Rheumatism, Croupous Pneumonia, and Influenza. Diseases of Children, Rhinology and Laryngology, and Otology. A perusal of these chapters will keep a practitioner well informed as to the modern trend of view in regard to the diagnosis, treatment, etc., of these various diseases. The work is a useful addition to most doctors' libraries.

The Mechanism of the Heart Beat, with Especial Reference to its Clinical Pathology. By THOMAS LEWIS, M. D., M. R. C. P., D. Sc., Lecturer in Cardiac Pathology, University College Hospital Medical School, Physician to Out-Patients, City of London Hospital for Diseases of the Chest. 295 pp., 213 figures, 5 plates. (*London and New York: Paul B. Hoeber, 1911.*)

This book gives a very complete summary of the present day knowledge of the origin and course of the cardiac impulse under normal and abnormal conditions, particularly in the disturbances of cardiac rhythm. It is practically a collection and systematic presentation of the author's own studies with the electrocardiograph under normal and pathological conditions both clinical and experimental, and these have been sufficiently extensive to furnish material for such a monograph. Dr. Lewis' most important contribution to cardiac physiology has been the demonstration that the auricular (P) wave of the normal electrocardiogram indicates that the impulse for the auricular systole arises in the vicinity of the superior veno-auricular junction at the site of the sino-auricular bundle of Wenckebach and the node which had been described by Keith and Flack. His proof consists in the fact that extrasystoles from stimulation of this region give a P wave of normal form, while those arising from stimulation of other regions

in either auricle have an abnormal form, often a complete inversion of the P wave. He is thus able to differentiate in clinical cases between these two different forms of auricular extrasystoles, the "homogenetic" arising at the node of Keith and Flack, and the "heterogenetic" arising at some abnormal site; and he has found that many disturbances of cardiac rhythm in man, such as extrasystolic arhythmias and paroxysmal tachycardia, are due to the occurrence of such heterogenetic impulses.

Dr. Lewis gives an excellent discussion of the nature of the absolute arhythmia (formerly termed nodal rhythm by Mackenzie, arhythmia perpetua by Gerhardt, and pulsus irregularis perpetuus by Hering). In this field he has rendered excellent service by confirming the suggestion of Cushny and Edmunds and the electrocardiographic demonstrations of Rothberger and Winterberg, showing that the disturbance of rhythm is brought about by fibrillary contractions of the auricles which send impulses down to the ventricles at varying intervals. The material of over one hundred cases under the author's observation is carefully analyzed, and the frequency of mitral stenosis as a predisposing factor is shown. It is in this form of arhythmia that digitalis is especially useful, acting by preventing some of the impulses from reaching the ventricles. Dr. Lewis gives an excellent chapter on Adams-Stokes Disease and another upon the action of the vagus.

Paroxysmal tachycardia he regards as due entirely to coördinated heterogenetic impulses arising in auricles whose irritability is increased; but believes that a regular tachycardia is never produced by fibrillation of the auricles, though admitting that the latter condition represents merely a grade of irritability higher than that seen in heterogenetic tachycardia. The latter fact was shown by the reviewer in 1908 but the author does not refer to this earlier work. (Several cases of paroxysmal tachycardia with jugular pulse of the ventricular type, reported from Dr. Lewis' clinic since the appearance of the book, show absence of the auricular P wave and present some similarity to auricular fibrallation, so that the question as to whether auricular fibrillation always brings about an irregular pulse as claimed by Dr. Lewis or whether it may in some cases give rise to this type of tachycardia as suggested by the reviewer, seems still an open one.) Not the least of Dr. Lewis' contributions is the demonstration that paroxysmal tachycardia can be produced in animals by ligation of a coronary artery as well as it can be by faradization of the auricles or by the administration of drugs.

The book is beautifully illustrated with original electrocardiograms and ordinary graphic records obtained from both clinical cases and laboratory experiments and a number of good diagrams and there are unusually good figures of the sino-auricular node and auriculoventricular bundle.

The style is clear and the self-confidence which is so common to British writers tends to brush aside everything that is ambiguous and to contribute much to its readable quality. Nevertheless, the reader should not be blinded to the fact that many theories though dogmatically expressed by the best of investigators may lead but a transitory existence. The bibliography though not complete is adequate for the treatment of the subject matter in hand. All in all the book is certainly the most complete treatise in existence upon the phase of cardiac pathology with which it deals and we can warmly recommend it to all who desire to acquaint themselves with the physiology and pathology of the normal and irregular heart.

A. D. HIRSCHFELDER.

Practical Anatomy. The Student's Dissecting Manual. By F. G. PARSONS, F. R. C. S. Eng., etc., and WILLIAM WRIGHT, F. R. C. S. Eng., etc. In Two Volumes. $2.40. (*New York: Longmans, Green & Co.; London: Edward Arnold, 1912.*)

There is no small type used in these volumes because unimportant details have been omitted, and "because in our experience" as the authors state in their preface "students usually pay more attention to the minutiæ contained in it [small type] than they do to the essential facts embodied in the large print." If this is true the English student must differ very essentially from other students. Every professor of anatomy must decide for himself what the unimportant details are, or what anatomical facts may be omitted from a student's text book on this subject, but we feel sure that it is rather the method of teaching anatomy which is at fault, than the extent and difficulty of the subject which explains the ignorance of most students when they are examined in anatomy. To write a book to make anatomy easy is a hopeless task and any comparatively brief work like this one can hardly give the student a thorough grasp of the subject. Gray's Anatomy in English still reigns supreme, and as this work has been constantly brought up-to-date, the student who has fifteen months to give to anatomy as in the English schools can afford a more comprehensive work than Parson and Wright's, many of whose illustrations seem to us only fairly satisfactory.

A Cyclopedia of American Medical Biography. Comprising the Lives of Eminent Deceased Physicians and Surgeons from 1610 to 1910. By HOWARD A. KELLY, M. D. Illustrated with portraits. Two volumes. (*Philadelphia and London: W. B. Saunders Company, 1912.*)

The indebtedness of the medical profession to Dr. Kelly is great for his unselfish efforts to perpetuate the lives and labors of upwards of twelve hundred medical men of more or less eminence who have lived and labored in America during the past three centuries.

The biographies are short and concise and content themselves for the most part with furnishing the material facts of the life and history of physicians deemed worthy of mention. Now and then a strain of overwrought eulogy may be noted which suggests that a rhetorical flower may have been plucked from the tributes placed by fond friends upon the grave of some much-beloved physician. This, however, is rare. The biographies are especially written for the work or compiled from original sources and the thick volumes constitute a reliable and accurate store-house of facts. The author's purpose has been to give a brief outline of every medical man who has been distinguished as a "thinker, writer, teacher or leader." The biographies are generally models of good taste and the names have been judiciously chosen. Some omissions are to be noted and doubtless some differences of opinion will always develop among those who select names worthy to be included in such a cyclopedia. There is always a tendency in works of this character to record the deeds of the surgeon or brilliant specialist and to pass over those of the no less skillful and scientific general practitioner which may be less pyrotechnic in character and do not lend themselves to history. In the books before us the proportion of physicians as compared with surgeons and specialists is about three-fifths to two-fifths. It is interesting to observe that the great majority of the latter are the product of the last century. There was a time when the general medical practitioner was also a surgeon and possibly a dentist or an eye specialist. Nathan Smith, who founded four medical schools and filled most of the chairs in several of them, treated typhoid fever successfully by the original and novel method of cold bathing; he was also a bold and fearless surgeon and in addition operated for cataract whenever occasion presented itself. We notice the omission of the names of N. S. Davis, of Chicago, the founder of the American Medical Association, of Eli Todd, of Hartford, who was a mighty force in the development of public sentiment towards building institutions for the insane, of Henry J. Bigelow, of Boston, of Henry B. Sands, of New York, and others.

The cyclopedia is in marked contrast to the ambitious work of Gross which consisted of a few biographies given with much detail, the more concise work of Atkinson or the journalistic commercialized effort of Stone to constitute every man his own biographer.

Here the biographies have been edited with evident care and much literary acumen. The full bibliographies appended to each biography is an excellent feature.

The preliminary essays nine in number by Bardeen, Tinker, Alleman, Kelly, Winfield, Friedenwald, Delavan, Withington and Shasted are of unequal value but several are of great interest. They relate to "Anatomy," "Surgery," "Gynecology and Obstetrics," "Dermatology," "Ophthalmology," "Laryngology," "Women in Medicine" and "Medical Jurisprudence." The reader can but wish that similar essays on "Medicine," "Pathology," "Physiology" and "Psychiatry" had been added as of more general interest and importance than several which have been presented.

These suggestions, however, are minor criticisms and do not detract from the preeminent value of the book which deserves a large sale. The illustrations are excellent and the letter-press is attractive.

A Manual of Surgical Treatment. By Sir W. Watson Cheyne, Bart., F. R. C. S., F. R. S., etc., and F. R. Burghard, M. S. (Lond.), F. R. C. S., etc. New (2d) edition. Thoroughly revised and largely rewritten. In five volumes, containing about 3000 pages and illustrated with about 900 engravings. $6.00 per volume. (*Philadelphia and New York: Lea & Febiger, 1912.*)

This system of surgery, for it may well be called so in spite of the title, is the third large system in English which has appeared within a short time, and the smaller surgeries that have been printed in the last year or two are innumerable, not to mention all the works in special branches of this art, so that it becomes more and more difficult to recommend any one book to a student or practitioner of limited means. In these days of rush also few have time to thoroughly digest all the good mental food that is offered them, and it is in a sense to be regretted that the publishers are so active. It is, however, a pleasure to see a good old book reprinted, and, therefore, the profession is to be congratulated on the republication of Sir Watson Cheyne's manual, whose merits have well recognized. No real student of surgery can fail to want to know what surgeons in other countries than his own are doing and thinking, and the careful reader of this work will acquire new ideas and so become a better operator. The first volume is divided into five parts: (1) Inflammation and its Sequelæ; (2) Wounds and Their Complications; (3) Syphilis and Tuberculosis; (4) Tumors; (5) Deformities and an Appendix of two chapters on Anæsthetics and The Examination of the Blood in Surgical Conditions. Volume II is arranged in three divisions: (1) The Surgical Affections of the Soft Tissues, divided into thirteen chapters dealing with affections of the skin and subcutaneous tissues, of the nails, of the lymphatic vessels and glands, of fasciæ, bursæ, muscles, tendon sheaths, tendons, nerves, veins, arteries and aneurisms; (2) The Surgical Affections of the Bones in fourteen chapters beginning with one on General Considerations, followed by others on fractures of clavicle and scapula, humerus, forearm and hand, pelvis, femur, patella, leg and foot, acute and chronic inflammation of bones, necrosis and phosphorus necrosis, tuberculosis and actinomycosis, syphilitic and rheumatic affections, rickets and scurvy rickets, disorders of ossification, and tumors of bones; and (3) Amputations in three chapters of General Considerations and amputations of the upper and lower extremity. There is a great deal of ground, and many most important topics dealt with in this volume, and some of the chapters are brief, but on the whole the proportion of the different subjects is well maintained. The illustrations, though not brilliant, are sufficiently clear to demonstrate what is intended. Both volumes are indexed. Although the volume is too heavy, yet the publishers are to be thanked for not having made this manual so unnecessarily clumsy, as are the American systems, whose large volumes are an abomination. This system will long hold a prominent position among works on surgery by English writers, serving as a safe and clear guide to the young surgeon.

The Surgery of Oral Diseases and Malformations. Their Diagnosis and Treatment. By George Van Ingen Brown, D. D. S., M. D., etc. Illustrated. $6.00. (*Philadelphia and New York: Lea & Febiger, 1912.*)

As the gynecologists no longer confine themselves to the surgery of the female pelvic organs, but reach out to the kidney, gallbladder, etc., so the dentists are now reaching out from the teeth, and to them the medical profession owes already marked advance in the treatment of fractured jaws. Here we have a surgery on all oral diseases by a dentist, as well as a surgeon, a happy combination, and one which gives the book a distinctive character of its own. The author discusses pathological dentition, infectious diseases, diseases of the mucous membrane of the mouth, of the nervous system affecting the buccal region, of bone, of glands, tumors, diseases of the maxillary sinus, diseases, tumors and malformations of the tongue, nasal deformities and diseases in relation to the maxillæ, diseases, injuries and malformations of the lips, and harelip, cleft-palate, and defects of speech. The work is an extensive one and well illustrated with a few color prints. We might wish that so many surgeons did not feel it incumbent on them to introduce their works with a chapter on anæsthesia. The subject is too broadly handled by the author to be of real value, and this we feel to be the characteristic of his work. Had he not attempted to cover so much ground or had he gone more into detail in some parts, the book would have been better. As it stands however it will fill a want and prove very serviceable to a large body of students. The internist as well as the surgeon can get many good hints from it as to obscure conditions involving the mouth.

National Association for the Study and Education of Exceptional Children. Proceedings of the Second Annual Conference, 1911.

The care of the exceptional or backward child is certainly one of the most important problems that we have to deal with and social workers interested in the moral welfare of these children, who are often degenerates, will find helpful suggestions in the various papers here presented and classified under three headings: (1) Causes of Exceptional Development in Children; (2) Educational Needs of the Various Kinds of Exceptional Children; and (3) The Exceptional Child as a Social Problem. This is not a problem by itself but closely woven into other social problems, such as syphilis, alcoholism, tuberculosis, poverty, etc., so that the exceptional child can and should be studied from many different points of view. As good English this is a most unfortunate use of the word "exceptional" and the society should we think alter its name.

Die Methoden der Untersuchung des Magens und Ihre Diagnostische Verwertung. Von Dr. Emil Schütz, Privatdozent an der Universität Wien. $2.75. (*Berlin und Wien: Urban & Schwarzenberg; New York: Rebman Company, 1911.*)

This is not simply a work dealing with the methods of gastric examinations but also a guide to the use of these methods in the differential diagnosis of diseases of the stomach. The author classifies his subject under the following headings: (1) Anamnesis; (2) The physical methods of gastric examinations; (3) Securing and examining the gastric contents; (4) Examination of the gastric contents without use of the stomach tube; (5) Examination of the functions of the stomach; and (6) X-ray examination of the stomach. He adds two chapters on the importance of blood and urine examinations in the diagnosis of diseases of the stomach, and one on the biologic methods to be

applied in the diagnosis of carcinoma. Dr. Schütz discusses not alone the application and use of older and newer methods but what makes the monograph valuable, he gives the result of his 30 years personal experiences with these. He lays especial stress on the estimation of the hydrochloric acid of the stomach and thinks that in spite of the doubt that some authors have expressed recently as to the value of determining its presence and amount, it none the less is a distinct aid in diagnosis. Palpation of the stomach has in his opinion not received the attention it deserves, but other means of examining the stomach like gastroscopy, gastrodiaphany he passes over briefly as having proved themselves of little worth. To those interested in gastric diseases this book will be serviceable.

Makers of Man. A Study of Human Initiative. By CHARLES J. WHITBY, M. D. (Cantab.) $3.00. (*New York: Rebman Company, 1911.*)

From the preface we learn that the author has "essayed the experiment of dealing with the lives of great men as problems capable, through and through, of psychological treatment and elucidation. Even their physical organisms are, from this point of view, to be regarded not as mere animated 'matter,' but each one as organized experience, a psychosis, the sub-conscious and super-conscious factors of which all play their part in contributing to the feeling tone, modifying the opinions, or determining the motives of conduct." The subjects chosen are forty world-famous individuals.

The book consists of thirteen chapters, four of which are continuations, and these are headed: Introductory, Classification, Family History, Parentage and Constitution, Physical Characteristics, Natural Vocation, The Natural History of Purpose, Power in the Crucible, Limitation and Crime, and Individuality: Its Nature and Power.

The above may be considered as viewpoints from which the author considers the lives of Julius Cæsar, Charlemagne, William the Silent, Sir Francis Drake, Cardinal Richelieu, Oliver Cromwell, Frederick the Great, Lord Nelson, Napoleon Bonaparte, Abraham Lincoln, Dante, Leonardo da Vinci, Titian, Cervantes, Mozart, Goethe, Beethoven, Sir Walter Scott, Turner, Gustave Flaubert, Bacon, Galileo, Harvey, Descartes, Spinoza, Sir Isaac Newton, Leibnitz, Kant, Hegel, Charles Darwin, Jesus Christ, St. Paul, Marcus Aurelius, St. Augustine, St. Gregory the Great, Mahomet, St. Francis d'Assisi, Martin Luther, Ralph Waldo Emerson, and Ernest Renan. Surely, excellent material.

The author has given us an intensely interesting book besides one of great value to the physician, psychologist, sociologist, eugenist, etc. The work has been excellently and most successfully done, and should be in the library of everyone interested in the uplift of the race or individual. Even one who is merely in search of entertaining reading will be well repaid by its perusal.

W. R. D.

Report of the International Plague Conference. Held at Mukden, April, 1911. (*Manila Bureau of Printing, 1912.*)

The feature of this report which stamps it with exceptional interest is the fact that the Conference was called by the Chinese Government and that Chinese physicians took an active part in the discussions. This demonstrates in a striking way the advance of the medical practitioner in China, and as time goes on there is not the least doubt but that important contributions to medicine will come from that country. Perhaps the most remarkable characteristic of the plague epidemic which existed in Manchuria and northern China in 1910-11 was its pneumonic form—the bubonic form practically not occuring at this time. The disease was doubtless contracted by hunters from a species of marten, known as the tarbagan, and spread from the hunters to the coolie class, which was the one that suffered most. The report which covers the bacteriology, pathology, clinical data, epidemiology, measures employed to combat the disease, etc., has been admirably prepared by Dr. Richard P. Strong, and will serve as the basis for all future reports on epidemic pneumonic plague. Thus the Conference will have proven of lasting benefit to the world.

Infantile Paralysis in Massachusetts During 1910. Together with Reports of Spinal Investigations Made in 1911 Bearing upon the Etiology of the Disease and the Method of its Transmission. (*Boston: Wright & Potter Printing Co., State Printers, 1912.*)

This report is reprinted from the Monthly Bulletins of the Massachusetts State Board of Health, and makes a most important addition to the literature of Infantile Paralysis. It is a great satisfaction to have the papers, some of which have appeared previously in various medical journals, thus reprinted with an abundance of illustrative maps. All interested in the epidemiology, as well as other features of the disease, will find this report most instructive.

The Prevention of Dental Caries. By J. SIM WALLACE, M. D., L. D. S., etc. Second Edition. 1/6. (*London: Office of The Dental Record, 1912.*)

The author's studies have led him to the belief that caries is due, in large measure at least, to the "highly refined carbohydrate foods," while "foods of a more fibrillar or fibrous character," which he calls "detergent," are less likely to induce this trouble. The latter help to cleanse the teeth during the chewing process, while the former stick to the teeth and are not easily removed. It is questionable whether this is the fundamental cause of caries, but, in any case, it seems likely to play a part, and if this small volume teaches its readers nothing more than the necessity of the constant use of a tooth brush it will serve a good end.

A Handbook of Practical Treatment. Edited by JOHN H. MUSSER, M. D., LL. D. and A. O. J. KELLY, A. M., M. D. Volume III. (*Philadelphia: W. B. Saunders Company, 1912.*)

The review of this book had just been completed when the news of the death of Dr. Musser was received. It is a sad coincidence that both of the editors of this work should have died so soon after its completion. There were few men more beloved by the profession than Dr. Musser. He was above all the clinician so far as concerned his professional work, but apart from this, his interest in the younger men of the profession was always strong. The untimely death of Dr. Kelly was a great loss to American medicine, but he has left his mark on the medical literature of his generation.

The third and final volume of this work keeps up the standard set by the previous ones. Constitutional diseases, those of the respiratory, digestive, urinary and nervous systems, and mental diseases are discussed. In a work such as this it is not possible to review every part in detail. The section dealing with constitutional diseases gives a very complete discussion of the treatment of these difficult problems. Dr. Futcher has written several of the sections in his usual clear and thorough manner. His reference to chronic rheumatism is to be highly commended. In the discussion of the diseases of the respiratory system several subjects were taken by the senior editor, whose discussion of them is full and satisfactory. In the section on gastric neuroses more attention might have been given to the importance of treatment of the general condition; reference is made to it, but this is one of the important points which would be the better of greater emphasis. We are too much given to paying attention to the relief of symptoms and losing sight of the essential causal condition and perhaps to no group of disorders does this apply with more force than to

the gastric neuroses. The trouble is usually more with the patient than with his stomach. Dr. Stockton contributes an excellent section on diseases of the liver which covers the subject very fully. A very important question—that of visceroptosis—is discussed by Dr. Sailer. This is well worthy of commendation and discusses a difficult subject very fully and well. Dr. Spiller takes the organic diseases of the nervous system and Dr. Taylor, the spinal meninges and cord. These articles are comparatively short but seem quite adequate. Dr. Dercum deals with the functional nervous disorders in a very satisfactory way.

Throughout the work the discussion of the surgical treatment is taken up fully and the editors have been fortunate in the men chosen for this. These sections are satisfactorily done throughout. It is becoming more and more the custom to take up the "borderland" subjects from both the medical and surgical sides, and very properly so. In the past there has been too little coöperation.

The work as a whole is a great addition to our literature on therapy and can be confidently recommended as a guide in treatment.

The Medical Annual. A Year Book of Treatment and Practitioner's Index. Thirtieth year. 9/6. (*Bristol: John Wright & Sons, Ltd., 1912.*)

This Annual is prepared with care by a large number of practitioners in various countries (England, France, Austria, India, the United States). Surgery and Medicine are both well covered, as one can judge from the fact that there is a chapter on Ionic Medication, one of the very latest developments in medicine. It is supplied with an excellent index, and numerous useful illustrations. There is much information in the volume of use only to the British practitioner, but anyone anxious to learn the progress that has been made in any special branch of medicine during the past year will find this volume most serviceable. The Annual is an excellent reference handbook.

The International Medical Annual. A Year Book of Treatment and Practitioner's Index. Thirtieth Year. $3.50. (*New York: E. B. Treat & Company, 1912.*)

This is merely the American edition of the Year Book of Treatment noted above, with the parts alone of service to English practitioners omitted.

Lateral Curvature of the Spine and Round Shoulders. By Robert W. Lovett, M. D. Second Edition. Revised and Enlarged. Illustrated. $1.75. (*Philadelphia: P. Blakiston's Son & Co., 1912.*)

Those who know the first edition of this work will want the second. It is a work designed essentially for the orthopedist, and no one in America has given more attention to this special branch of medicine than Lovett. From the careful anatomical and clinical studies made by him, his conclusions should be attentively studied by those working in the same field. If more physicians and surgeons would write similar monographs, instead of attempting to cover the whole field of medicine and surgery, many more valuable treatises would be published than appear now. Here is a subject well handled by one who has studied it most thoroughly and made himself master of its difficulties.

Surgical Operations. A Hand-Book for Students and Practitioners. By Prof. Friedrich Pels-Leusden, Berlin. Only Authorized English Translation by Faxton E. Gardner, M. D., New York. Illustrated. (*New York: Rebman Company, 1912.*)

The Rebman Company is doing a valuable piece of work in furnishing translations, to American doctors, of important foreign medical books, and "Surgical Operations" is one of the best of its series. As chief surgeon to one of the largest surgical clinics in Berlin, Pels-Leusden writes from a large and varied experience, and it is of distinct advantage for men who cannot travel or read foreign languages to have this opportunity to study the views of one of the leading operators of Europe. There is no lack of excellent surgeries both for the student and practitioner, but many will be glad to add this book to their libraries. After introductory chapters on Antisepsis and Asepsis, Anæsthesia, and Division and Reunion of the Different Tissues, the author takes up the Surgery of the Blood-vessels, Operations on the Extremities, Operations on the Head, Neck, Chest, Surgery of the Abdomen, and Urinary and Genital Organs. It is a typical German production in the vague lack of reference to the work of foreigners, but this in a way makes the book more valuable as representing modern German surgery, and to change but slightly a phrase in the author's preface, "those who will seek advice in this book will find its reading fruitful." It is a well-illustrated work of about 700 pages with good type and paper.

Infections of the Hand. A Guide to the Surgical Treatment of Acute and Chronic Suppurative Processes in the Fingers, Hand, and Forearm. By Allen B. Kanavel, M. D. Illustrated with 133 Engravings. $3.75. (*Philadelphia and New York: Lea & Febiger, 1912.*)

The book is divided into two parts. The first deals with simple localized infections and allied minor clinical entities. The second takes up grave infections, as follows: (a) Discussion of diagnosis and treatment in general; (b) Tenosynovitis and fascial space abscesses; (c) Acute lymphangitis and allied infections; (d) Complications and sequelæ of acute infections.

The work is based on careful experimental and anatomical investigations in conjunction with accurate clinical observations on a large number of cases.

Infections of the hand and forearm are very common and nearly every medical man feels competent to take care of such cases. However, many of these infections are treated without regard to definite anatomical knowledge of the part, and while a number of them recover with a functional result which is sometimes good, on the other hand we all see results which are distinctly bad, and which are due, in many instances, to a lack of knowledge of the structures and spaces involved.

The book is well gotten up and the illustrations are excellent. The descriptions are for the most part clear.

It is, indeed, a pleasure to read such a thorough exposition of a subject, and Dr. Kanavel is to be congratulated on this valuable piece of work. The volume should be in the library of every surgeon and will also be of great use to the general practitioner.

J. S. D.

Surgery of Deformities of the Face, Including Cleft-Palate. By John B. Roberts, A. M., M. D., etc. Illustrated. $3.00. (*New York: William Wood & Co., 1912.*)

This work founded on the Mütter Lectures of the College of Physicians of Philadelphia, delivered by the author in 1900 will be of assistance to all surgeons. Plastic operations are among the most difficult that a surgeon meets with, and this accounts in some measure for the lack of development in this branch of surgery—though it seems also as if it required a man with very special gifts of patience, foresight, and delicacy of hand, to obtain good results in such work. One necessarily hesitates to attack a severe deformity of the face lest the patient may not only be no better but possibly worse off after the operation. Careful study of Roberts' book will help many a surgeon in a tight place, and it is so well and abundantly illustrated that the operator who for the first time tackles one of these delicate cases will find here all the assistance he can obtain in any book—for his success he must have those same gifts which the author has, as shown in his results.

An Index of Differential Diagnosis of Main Symptoms. By Various Writers. Edited by HERBERT FRENCH, M. D. Oxon., etc. Illustrated. 30/. (*Bristol: John Wright & Sons, Ltd., 1912.*)

A few sentences from the preface will best indicate the scope of this comprehensive work. "The book is a treatise on the application of differential diagnosis to all the main signs and symptoms of disease . . . . It covers the whole ground of medicine, surgery, gynecology, ophthalmology, dermatology, and necrology. . . . Its articles on various symptoms are arranged in alphabetical order. Whilst . . . . the general index at the end gathers these together under the headings of the various *diseases* in which they occur." As the editor points out both text and index should be used together, as otherwise the reader may miss a number of places in which diagnosis is discussed, for each symptom is classified but once under its own head, while a disease may be referred to many times under different symptoms. Many prominent English physicians have contributed to this volume, as Bosanquet, Buzzard, Cammidge, Garrod, Hertz to mention only a few well-known names, but these are sufficient to indicate that the work has been done with thoroughness by leaders in their specialties. There is no doubt that a book as carefully prepared as this has been will prove very serviceable, especially to students and young practitioners; and in obscure cases, to the older practitioner also. The different sections are signed by their respective authors, which adds, we feel, weight to the articles. This Index is a valuable addition to the armamentarium of the physician, and both the editor and his collaborators deserve hearty praise for the successful accomplishment of this exhaustive undertaking. The publishers are also to be complimented on their part of the work—the type is necessarily small, but it is clear, and the illustrations are satisfactory.

BOOKS RECEIVED.

London Practitioners' Manuals. Anæsthesia and Analgesia. By J. D. Mortimer, M. B. (Lond.), F. R. C. S. (Eng.). 1911. 16°. 276 pages. University of London Press, London.

London Practitioners' Manuals. Minor Surgery. By Leonard A. Bidwell, F. R. C. S. With eighty-eight illustrations. 1911. 16°. 265 pages. University of London Press, London.

American Gynecological Society. Transactions. Volume 36, for the year 1911. 8vo. 605 pages. Philadelphia.

Studies from the Rockefeller Institute for Medical Research. Reprints. Volume XIII. 1911. 8vo. New York.

Index-Catalogue of the Library of the Surgeon-General's Office, United States Army. Authors and Subjects. Second series. Vol. XVI. Skinko-Stysanus. 1911. 4to. 882 pages. Washington.

Serum Diagnosis of Syphilis and the Butyric Acid Test for Syphilis. By Hideyo Noguchi, M. D., M. Sc. 14 Illustrations. Second edition. 1911. 8vo. 238 pages. J. B. Lippincott Company, Philadelphia and London.

Progressive Medicine. A Quarterly Digest of Advances, Discoveries and Improvements in the Medical and Surgical Sciences. Edited by Hobart Amory Hare, M. D., assisted by Leighton F. Appleman, M. D. Volume IV. December, 1911. 8vo. 326 pages. Lea & Febiger, Philadelphia and New York.

The Bellevue Hospital Nomenclature of Diseases and Conditions. With Rules for the Recording and Filing of Histories. Compiled by the Committee on Clinical Records, composed of Robert J. Carlisle, M. D., Warren Coleman, M. D., Thomas A. Smith, M. D., Edmund L. Dow, M. D. Adopted by the Board of Trustees, 1903. Revised and made to conform to the International Classification. 1911. 16°. 328 pages. New York.

Nachweis und Bestimmung von Giften auf biologischem Wege. Eine Anleitung für Pharmakologen, Gerichtsärzte, Gerichtschemiker und Apotheker. Von Dr. phil. et med. Hermann Fühner. Mit 89 zum Teil farbigen Textabbildungen. 1911. 8vo. 176 pages. Urban & Schwarzenberg, Berlin und Wien; Rebman Company, New York.

Urology. The Diseases of the Urinary Tract in Men and Women. By Ramon Guiteras, M. D. (Harv.). With nine hundred and forty-three illustrations in text and seven plates. 1912. 8vo. Two Volumes. D. Appleton & Co., New York and London.

A Treatise on Tumors. By Arthur E. Hertzler, M. D., Ph. D. Illustrated with 538 engravings and 8 plates. 1912. 4to. 725 pages. Lea & Febiger, Philadelphia and New York.

Die experimentelle Pharmakologie als Grundlage der Arzneibehandlung. Von Dr. Hans H. Meyer und Dr. R. Gottlieb. Zweite, neubearbeitete Auflage. Mit 64 zum Teil farbigen Textabbildungen und 1 farbigen Tafel. 1911. 8vo. 554 pages. Urban & Schwarzenberg, Berlin und Wien; Rebman Company, New York.

Second Review of Some of the Recent Advances in Tropical Medicine, Hygiene and Tropical Veterinary Science. Being a Supplement to the Fourth Report of the Wellcome Tropical Research Laboratories at the Gordon Memorial College, Khartoum. By Andrew Balfour, M. D., B. Sc., F. R. C. P., Edin., D. P. H. Camb. and Captain R. G. Archibald, M. B., R. A. M. C. in collaboration with Captain W. B. Fry, M. R. C. S., L. R. C. P. and Captain W. R. O'Farrell, L. R. C. P. & S. I., R. A. M. C. 1911. 4to. 448 pages. Published for Department of Education, Sudan Government, Khartoum, by Baillière, Tindall & Cox, London; Toga Publishing Company, New York City.

The Surgery of Oral Diseases and Malformations. Their Diagnosis and Treatment. By George Van Ingen Brown, D. D. S., M. D., C. M. Illustrated with 359 engravings and 21 plates. 1912. 8vo. 740 pages. Lea & Febiger, Philadelphia and New York.

Honan's Handbook to Medical Europe. A Ready Reference Book to the Universities, Hospitals, Clinics, Laboratories and General Medical Work of the Principal Cities of Europe. By James Henry Honan, M. D. With maps of Berlin, Edinburgh, London and Paris. 1912. 12mo. 261 pages. P. Blackiston's Son & Co., Philadelphia.

Ergebnisse der Chirurgie und Orthopädie. Herausgegeben von Erwin Payr, Hermann Küttner. Vierter Band. Mit 221 Textabbildungen. 1912. 8vo. 702 pages. Julius Springer, Berlin.

Progressive Medicine. A Quarterly Digest of Advances, Discoveries and Improvements in the Medical and Surgical Sciences. Edited by Hobart Amory Hare, M. D., assisted by Leighton F. Appleman, M. D. Volume I. March, 1912. 8vo. 377 pages. Lea & Febiger, Philadelphia and New York.

Filariasis and Elephantiasis in Fiji. Being a Report to the London School of Tropical Medicine. By P. H. Bahr, M. A., M. B., B. C., D. T. M. & H., Cantab., M. R. C. S., Eng., L. R. C. P., Lond. With many colored and monochrome plates, numerous charts and a map. 1912. 4to. 182 pages. Witherby & Co., London.

International Clinics. A Quarterly of Illustrated Clinical Lectures and Especially Prepared Original Articles. Edited by Henry W. Cattell, A. M., M. D. Volume I. Twenty-second Series. 1912. 8vo. 304 pages. J. B. Lippincott Company, Philadelphia and London.

A Manual of Surgical Treatment. By Sir W. Watson Cheyne, Bart., C. B., D. Sc., LL. D., F. R. C. S., F. R. S. and F. F. Burghard, M. S. (Lond.), F. R. C. S. New edition, entirely revised and largely rewritten with the assistance of T. P. Legg, M. S. (Lond.), F. R. C. S., and Arthur Edmunds, M. S. (Lond.), F. R. C. S. In Five Volumes. Vol. I. *The Treatment of General Surgical Diseases, including Inflammation, Suppuration, Ulceration, Gangrene, Wounds and their Complications, Infective Diseases and Tumors, Deformities.* 1912. 8vo. 552 pages. Lea & Febiger, Philadelphia and New York.

A Mother's Guide. A Manual for the Guidance of Mothers and Nurses. By Francis Tweddell, M. D. [1911.] 16°. 182 pages. James T. Dougherty, New York.

Practical Anatomy. The Student's Dissecting Manual. By F. G. Parsons, F. R. C. S., Eng., and William Wright, M. B., D. Sc., F. R. C. S., Eng. In Two Volumes. Vol. I. *The Head and Neck: the Lower Extremity.* Vol. II. *The Thorax: Abdomen: Pelvis: Upper Extremity.* 1912. 12°. Longmanns, Green & Co., New York; Edward Arnold, London.

A Manual of First Aid. For Laymen, with Special Reference to Industrial Accidents. By Ernest A. Wells, M. D. [1911.] 8vo. 48 pages. Aetna Life Insurance Company, Hartford, Conn.

Surgical Operations. By Prof. Friedrich Pels-Leusden. Only authorized English translation by Faxton E. Gardner, M. D. With six hundred and sixty-eight illustrations. [1912.] 4to. 726 pages. Rebman Company, New York.

Fourth Scientific Report on the Investigations of the Imperial Cancer Research Fund. Under the Direction of the Royal College of Physicians of London and the Royal College of Surgeons of England. By Dr. E. F. Bashford. 1911. 8vo. 223 pages. Taylor & Francis, London.

International Clinics. A Quarterly of Illustrated Clinical Lectures and Especially Prepared Original Articles. Edited by Henry W. Cattell, A. M., M. D. Twenty-first Series. Volume IV. 1911. 8vo. 322 pages. J. B. Lippincott Company, Philadelphia and London.

Swamp Fever in Horses. By L. Van Es, E. D. Harris and A. F. Schalk. North Dakota Agricultural Experiment Station. Department of Veterinary Science. Bulletin No. 94. 1911. 8vo. Fargo, North Dakota.

Further Researches into Induced Cell-Reproduction and Cancer. Consisting of Papers by H. C. Ross, M. R. C. S., England, L. R. C. P., London, J. W. Cropper, M. B., M. Sc., Liverpool, and E. H. Ross, M. R. C. S., England, L. R. C. P., London. With Illustrations. The McFadden Researches, 1911. 8vo. 63 pages. John Murray, London; P. Blackiston's Son & Co., Philadelphia.

Manual of Operative Surgery. By John Fairbairn Binnie, A. M., C. M. (Aberdeen). Fifth edition, revised and enlarged. With 1365 illustrations, a number of which are printed in colors. 1911. 8vo. 1153 pages. P. Blackiston's Son & Co., Philadelphia.

Text-Book of Medical Jurisprudence and Toxicology. By John J. Reese, M. D. Eighth edition revised by D. J. McCarthy, A. B., M. D. 1911. 8vo. 660 pages. P. Blackiston's Son & Co., Philadelphia.

Transactions of the Association of American Physicians. Twenty-sixth session held at Altantic City, May 9 and 10, 1911. Volume XXVI. 1911. 8vo. 552 pages. Printed for the Association, Philadelphia.

Infections of the Hand. A Guide to the Surgical Treatment of Acute and Chronic Suppurative Processes in the Fingers, Hand, and Forearm. By Allen B. Kanavel, M. D. Illustrated with 133 engravings. 1912. 8vo. 447 pages. Lea & Febiger, Philadelphia and New York.

Transactions of the Medico-Chirurgical Society of Glasgow. (Glasgow Pathological and Clinical Society Amalgamated 1907.) Volume X. Session 1910-1911. Edited by R. Speirs Fullarton, M. A., M. D. 1911. 8vo. 162 pages. Alex. Macdougall, Glasgow.

Transactions of the American Surgical Association. Volume the Twenty-ninth. Edited by Archibald MacLaren, M. D., Recorder of the Association. 1911. 8vo. 496 pages. Printed for the Association, Philadelphia.

A Handbook of the Diseases of the Eye and Their Treatment. By Sir Henry R. Swanzy, A. M., M. D., D. Sc., and Louis Werner, M. B., F. R. C. S. I., Sen. Mod. Univ. Dub. Tenth edition. With illustrations. 1912. 8vo. 634 pages. P. Blackiston's Son & Co., Philadelphia.

Bellevue and Allied Hospitals, City of New York. Eighth Annual Report. 1909. 8vo. 88 pages. New York.

The Growth of Bone. Observations on Ostcogenesis. An Experimental Inquiry into the Development and Reproduction of Diaphyseal Bone. By William Macewen, F. R. S. 1912. 8vo. 210 pages. James Maclehose & Sons, Glasgow.

Nervous and Mental Disease Monograph Series No. 10. Handbook of Mental Examination Methods. By Shepherd Ivory Franz, Ph. D. With 33 figures and diagrams. 1912. 8vo. 165 pages. The Journal of Nervous and Mental Disease Publishing Company, New York.

Nervous and Mental Diseases. By Archibald Church, M. D., and Frederick Peterson, M. D. With 343 illustrations. Seventh edition, thoroughly revised. 1911. 8vo. 932 pages. W. B. Saunders Company, Philadelphia and London.

A Handbook of Practical Treatment. By Many Writers. Edited by John H. Musser, M. D., LL. D., and A. O. J. Kelly, A. M., M. D. Volume III. 1912. 8vo. 1095 pages. W. B. Saunders Company, Philadelphia and London.

Operative Obstetrics. Including the Surgery of the Newborn. By Edward P. Davis, A. M., M. D. With 264 illustrations. 1911. 8°. 483 pages. W. B. Saunders Company, Philadelphia and London.

The Surgical Clinics of John B. Murphy, M. D., at Mercy Hospital, Chicago. Volume I. No. 1. February 1, 1912. 8vo. 133 pages. W. B. Saunders Company, Philadelphia and London.

Motive-Force and Motivation-Tracks. A Research in Will Psychology. By E. Boyd Barrett, S. J. 1911. 8vo. 225 pages. Longmans, Green & Co., New York.

Fourth Report of the Wellcome Tropical Research Laboratories at the Gordon Memorial College, Khartoum. Volume A.—Medical. Andrew Balfour, M. D., B. Sc., F. R. C. P., Edin., D. P. H., Camb. Director. 1911. 4to. 404 pages. Published for Department of Education, Sudan Government, Khartoum, by Baillière, Tindall & Cox, London.

Brown University, Providence, Rhode Island. Contributions from the Biological Laboratory (formerly Anatomical Laboratory). Vol. VII. Issued October, 1911. Providence, Rhode Island.

The Johns Hopkins Hospital Bulletins are issued monthly. They are printed by the LORD BALTIMORE PRESS, Baltimore. Subscriptions, $2.00 a year (foreign postage, 50 cents), may be addressed to the publishers, THE JOHNS HOPKINS PRESS, BALTIMORE; single copies will be sent by mail for twenty-five cents each. Single copies may also be procured from the BALTIMORE NEWS CO., Baltimore.